Simvastatin Treatment Modulates Mechanically-Induced Injury and Inflammation in Respiratory Epithelial Cells. Higuita-Castro N, Shukla VC, Mihai C, Ghadiali SN. *Annals of biomedical engineering* 2016. Mechanical forces in the respiratory system, including surface tension forces during airway reopening and high transmural pressures, can result in epithelial cell injury, barrier disruption and inflammation. In this study, we investigated if a clinically relevant pharmaceutical agent, Simvastatin, could mitigate mechanically induced injury and inflammation in respiratory epithelia. Pulmonary alveolar epithelial cells (A549) were exposed to either cyclic airway reopening forces or oscillatory transmural pressure in vitro and treated with a wide range of Simvastatin concentrations. Simvastatin induced reversible depolymerization of the actin cytoskeleton and a statistically significant reduction the cell's elastic modulus. However, Simvastatin treatment did not result in an appreciable change in the cell's viscoelastic properties. Simvastatin treated cells did exhibit a reduced height-to-width aspect ratio and these changes in cell morphology resulted in a significant decrease in epithelial cell injury during airway reopening. Interestingly, although very high concentrations (25-50 microM) of Simvastatin resulted in dramatically less IL-6 and IL-8 pro-inflammatory cytokine secretion, 2.5 microM Simvastatin did not reduce the total amount of pro-inflammatory cytokines secreted during mechanical stimulation. These results indicate that although Simvastatin treatment may be useful in reducing cell injury during airway reopening, elevated local concentrations of Simvastatin might be needed to reduce mechanically-induced injury and inflammation in respiratory epithelia. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27411707

Monocyte Adhesion and Plaque Recruitment During Atherosclerosis Development Is Regulated by the Adapter Protein Chat-H/SHEP1. Herbin O, Regelmann AG, Ramkelawon B et al. *Atherosclerosis, thrombosis, and vascular biology* 2016. OBJECTIVE: The chronic inflammation associated with atherosclerosis is caused by lipid deposition followed by leukocyte recruitment to the arterial wall. We previously showed that the hematopoietic cell-specific adaptor protein Cas- and Hef1-associated signal transducer hematopoietic isofrom (Chat-H)/SHEP1 regulated lymphocyte adhesion and migration. In this study, we analyzed the role of Chat-H in atherosclerosis development. APPROACH AND RESULTS: Using Chat-H-deficient bone marrow transplantation in low-density lipoprotein receptor-deficient mice, we found that Chat-H regulated atherosclerotic plaque formation. Chat-H deficiency in hematopoietic cells associated with lower plaque complexity and fewer leukocytes in the lesions, whereas myeloid-specific deletion of Chat-H was sufficient for conferring atheroprotection. Chat-H deficiency resulted in reduced recruitment of classical Ly6chigh and nonclassical Ly6clow monocytes to the plaques, which was accompanied by increased numbers of both monocyte subsets in the blood. This was associated with defective adhesion of Chat-H-deficient Ly6chigh and Ly6clow monocytes to vascular cell adhesion molecule-1 in vitro and impaired infiltration of fluorescent bead-loaded monocytes to atherosclerotic plaques. In contrast, Chat-H was dispensable for CX3CL1 and CCR1/CCR5-dependent migration of monocytes. CONCLUSIONS: Our findings highlight Chat-H as a key protein that regulates atherosclerosis development by controlling monocyte adhesion.
and recruitment to the plaques and identify a novel target that may be exploited for treating atherosclerosis. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27417580


[4] Effect of rosuvastatin or its combination with omega-3 fatty acids on circulating CD34+ progenitor cells and on endothelial colony formation in patients with mixed dyslipidaemia. Chantzichristos VG, Agouridis AP, Moutzouri E *et al. Atherosclerosis* 2016; 251:240-247. BACKGROUND AND AIMS: Hypercholesterolaemia is associated with a reduced number of circulating progenitor cells, a defect that is restored by statin therapy. We studied the effect of rosuvastatin monotherapy or its combination with omega-3 polyunsaturated fatty acids (omega-3 PUFAs) on progenitor cell number and function in patients with mixed dyslipidaemia. METHODS: Fifty patients with mixed dyslipidaemia and fifty-five normolipidaemic, apparently healthy, age- and sex-matched volunteers participated in the study. Patients were randomized to receive a daily dose of either 40 mg rosuvastatin (R group, n = 26) or 10 mg rosuvastatin plus 2 g of omega-3 PUFAs (R + O group, n = 24). The number of circulating CD34+ and CD34+/KDR+ progenitor cells as well as the number of colony-forming units-endothelial cells (CFU-ECs) at 10 days of culture were assessed at baseline and 3 months post-treatment. RESULTS: The number of CD34+ and CD34+/KDR+ cells per 10,000 leukocytes as well as the number of CFU-ECs were significantly lower in both patient groups compared with healthy volunteers (all p = 0.03). A 3-month treatment with either R or R + O significantly increased circulating CD34+ and CD34+/KDR+ cells as well as the number of CFU-ECs compared with baseline (all p = 0.03). Importantly, the increase in the above parameters was inversely correlated with therapy-induced reduction in lipid parameters in both patient groups. CONCLUSIONS: Patients with mixed dyslipidaemia exhibit low numbers of circulating CD34+ and CD34+/KDR+ cells as well as CFU-ECs in culture, a defect restored by 3-month treatment with either high-rosuvastatin dose or a combination of low-rosuvastatin dose with omega-3 PUFAs. The pathophysiological meaning of our results regarding the increased cardiovascular risk in these patients remains to be established. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27415612

[5] Low-density lipoprotein cholesterol levels and lipid-modifying therapy prescription patterns in the real world: An analysis of more than 33,000 high cardiovascular risk patients in Japan. Teramoto T, Uno K, Miyoshi I *et al. Atherosclerosis* 2016; 251:248-254. BACKGROUND AND AIMS: Low-density lipoprotein cholesterol (LDL-C) is a key modifiable risk factor in the development of cardiovascular (CV) disease. In 2012, the Japan Atherosclerosis Society (JAS) issued guidelines recommending statins as first-line pharmacotherapy for lowering LDL-C in patients at high risk for CV events. This study assessed achievement of recommended LDL-C goals and lipid-modifying therapy (LMT) use in a high CV risk population in Japan. METHODS: Patients from the Medical Data Vision (MDV) database, an electronic hospital-based claims database in Japan, who met the following inclusion criteria were included in this study: LDL-C measurement in 2013; >/=20 years of age; >/=2 years representation in the database; and a
high CV risk condition (recent acute coronary syndrome (ACS), other coronary heart disease (CHD), ischemic stroke, peripheral arterial disease (PAD) or diabetes). LDL-C goal attainment was assessed based on LDL-C targets in the JAS guidelines. RESULTS: A total of 33,325 high CV risk patients met the inclusion criteria. Overall, 68% of the cohort achieved guideline recommended LDL-C targets, with only 42% receiving current treatment with statins. Attainment of LDL-C goals was 68% for ACS, 55% for CHD, and 80% each for ischemic stroke, PAD, and diabetes patients. Concomitant use of non-statin LMTs was low. CONCLUSIONS: In a high CV risk population in a routine care setting in Japan, guideline recommended LDL-C goal attainment and utilization of statins and other LMT was low. In addition, physicians appeared to be more likely to consider the initiation of statins in patients with higher baseline LDL-C levels.

[6] An evaluation of an aptamer for use as an affinity reagent with MS: PCSK9 as an example protein. Gupta V, Lassman ME, McAvoy T et al. Bioanalysis 2016.BACKGROUND: For quantitative immunoaffinity IA-LC-MS, the utility of antibodies has been demonstrated many times but the utility of aptamers as affinity reagents is unproven. METHODS: Immunoaffinity reagents including a monoclonal antibody and an aptamer were coupled to magnetic beads and used as part of an enrichment strategy for PCSK9 quantitation in plasma. RESULTS: With limited method development, we have established a comparison of an anti-PCSK9 aptamer with an anti-PCSK9 monoclonal antibody. The background that results from a tryptic digest of affinity enrichment in plasma was demonstrated for each reagent using high-resolution full scan MS. The assay recovery was demonstrated for multiple concentrations of aptamer in plasma with different concentrations of PCSK9 protein. CONCLUSION: The aptamer achieved comparable enrichment to the antibody, but with lower peptide background, thus demonstrating the potential use of aptamers for IA-LC-MS. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27419905

[7] Ursodeoxycholic acid impairs atherogenesis and promotes plaque regression by cholesterol crystal dissolution in mice. Bode N, Grebe A, Kerksiek A et al. Biochem Biophys Res Commun 2016.Atherosclerosis is a chronic inflammatory disease driven primarily by a continuous retention of cholesterol within the subendothelial space where it precipitates to form cholesterol crystals (CC). These CC trigger a complex inflammatory response through activation of the NLRP3 inflammasome and promote lesion development. Here we examined whether increasing cholesterol solubility with ursodeoxycholic acid (UDCA) affects vascular CC formation and ultimately atherosclerotic lesion development. UDCA mediated intracellular CC dissolution in macrophages and reduced IL-1beta production. In ApoE-/- mice, UDCA treatment not only impaired atherosclerotic plaque development but also mediated regression of established vascular lesions. Importantly, mice treated with UDCA had decreased CC-depositions in atherosclerotic plaques compared to controls. Together, our data demonstrate that UDCA impaired CC and NLRP3 dependent inflammation by increasing cholesterol solubility and diminished atherosclerosis in mice. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27416761
Amlodipine and atorvastatin improve ventricular hypertrophy and diastolic function via inhibiting TNF-alpha, IL-1beta and NF-kappaB inflammatory cytokine networks in elderly spontaneously hypertensive rats. Lu J, Liu F, Chen F et al. Biomedicine & pharmacotherapy = Biomedicine & pharmacotherapie 2016; 83:330-339. This study aimed to examine the effects of amlodipine and atorvastatin alone or in combination on the regulation of inflammatory cytokines and the underlying mechanisms in elderly spontaneously hypertensive (SH) rats. The level of serum hs-CRP was detected with ELISA. The serum TNF-alpha and IL-1beta levels were assessed by radioimmunity assay (RIA). Cardiac inflammatory cell infiltration was observed by HE staining. The protein levels of TNF-alpha, IL-1beta, of NF-kappaB P65 and IkappaBalpha were detected by immunoblotting. The intracellular localization of NF-kappaB p65 was observed using immunohistochemistry. Amlodipine or atorvastatin obviously ameliorated the myocardial inflammatory cell infiltration in SH rats, which was further improved by combinatorial treatment with amlodipine and atorvastatin. Either amlodipine or atorvastatin decreased plasma IL-1beta content in SH rats, but there was no significant difference when compared with untreated SH rats. However, the combination of amlodipine and atorvastatin significantly decreased plasma IL-1beta level in SH rats. Moreover, amlodipine or atorvastatin intervention significantly reduced myocardial TNF-alpha and IL-1beta protein levels in SH rats, which was further suppressed by the combination of amlodipine and atorvastatin. In addition, amlodipine or atorvastatin inhibited the activity of NF-kappaB signaling in SH rats, which was further suppressed by combinatorial treatment. Furthermore, amlodipine or atorvastatin restored the activity of IkappaB-alpha in SH rats, which was enhanced by combinatorial treatment. Our results demonstrated amlodipine and atorvastatin improved ventricular hypertrophy and diastolic function possibly through the intervention of TNF-alpha, IL-1beta, NF-kappaB/IkappaB inflammatory cytokine network. Our study suggests that amlodipine combined with atorvastatin may have additive effect on inhibiting inflammatory response. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27399810

Effect of 12-O-tetradecanoylphorbol-13-acetate-induced psoriasis-like skin lesions on systemic inflammation and atherosclerosis in hypercholesterolaemic apolipoprotein E deficient mice. Madsen M, Hansen PR, Nielsen LB et al. BMC dermatology 2016; 16:9. BACKGROUND: Risk of cardiovascular disease is increased in patients with psoriasis, but molecular mechanisms linking the two conditions have not been clearly established. Lack of appropriate animal models has hampered generation of new knowledge in this area of research and we therefore sought to develop an animal model with combined atherosclerosis and psoriasis-like skin inflammation. METHODS: Topical 12-O-tetradecanoylphorbol-13-acetate (TPA) was applied to the ears twice per week for 8 weeks in atherosclerosis-prone apolipoprotein E deficient (ApoE(-/-)) mice. RESULTS: TPA led to localized skin inflammation with increased epidermal thickness, infiltration of inflammatory-like cells and augmented tissue interleukin-17F levels. Systemic effects of the topical application of TPA were demonstrated by increased plasma concentration of serum amyloid A and splenic immune modulation, respectively. However, atherosclerotic plaque area and composition, and mRNA levels of
several inflammatory genes in the aortic wall were not significantly affected by TPA-induced skin inflammation. CONCLUSIONS: TPA-induced psoriasis-like skin inflammation in atherosclerosis-prone ApoE(-/-) mice evoked systemic immune-inflammatory effects, but did not affect atherogenesis. The results may question the role of psoriasis-induced inflammation in the pathogenesis of atherosclerosis in psoriasis patients. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27401543

[10] Dyslipidemia and Dementia. Tamaoka A. Brain and nerve = Shinkei kenkyu no shinpo 2016; 68:737-742. Several lines of evidences support a possible involvement of serum cholesterol in the development of dementia/Alzheimer's disease (AD), with hypercholesterolemia as one of the risk factors that can be targeted by therapeutic interventions. It has also been suggested that statins, prescribed as lipid-lowering drugs to patients at risk for cardiovascular conditions, may be useful in both the prevention and treatment of AD. Currently, conflicting evidences from epidemiological studies indicate a controversial association between dyslipidemia and dementia/AD risk. In randomized clinical trials, virtually no beneficial effect of statin therapy has been observed. On the other hand, in vitro and in vivo animal experiments have revealed that statins suppress amyloid beta protein (Abeta) generation. All these findings suggest that statins can be potentially used as preventive or therapeutic agents for AD. In addition, currently the pathophysiological process of AD is thought to begin many years before the diagnosis of AD dementia. Then, statin treatment as well as some disease-modifying therapies may be more efficacious at an early stage of AD including preclinical AD or mild cognitive impairment due to AD. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27395458

[11] Gene Polymorphisms Affect the Effectiveness of Atorvastatin in Treating Ischemic Stroke Patients. Yue YH, Bai XD, Zhang HJ et al. Cellular physiology and biochemistry : international journal of experimental cellular physiology, biochemistry, and pharmacology 2016; 39:630-638. BACKGROUND/AIMS: The aim of the present study is to investigate whether the single nucleotide polymorphism (SNP) in lipid metabolism related genes would affect the effectiveness of atorvastatin in both Han and Uighur populations. METHODS: 200 ischemic stroke patients were treated with atorvastatin. The differences of blood lipid level and their ratios were measured. Six lipid related genes, HMGCR, APOA5, LPL, CETP, LDLR and PCSK9 were selected as candidate genes. And nine SNP loci in these six genes were genotyped by SNaPshot technique. RESULTS: In all patients treated with atorvastatin, the SNP rs662799 significantly affected the ratio of x0394;LDL and x0394;LDL/LDL (p < 0.05); the SNP rs320 significantly affected the ratio of x0394;LDL/LDL and x0394;(LDL/HDL)/(LDL/HDL) (p < 0.01) and the SNP rs708272 significantly affected the ratio of x0394;LDL (p < 0.05). In Han population treated with atorvastatin, the SNP rs662799 significantly affected the ratio of x0394;LDL (p < 0.05); the SNP rs320 significantly affected the ratio of x0394;LDL/LDL and x0394;(LDL/HDL)/(LDL/HDL) (p < 0.01). In Uighur population treated with atorvastatin, the SNP rs2266788 significantly affected the ratio of x0394;HDL (p < 0.05); the SNP rs662799 significantly affected the ratio of x0394;LDL/LDL (p < 0.05) and the SNP rs708272 significantly affected the ratio of x0394;LDL (p <
0.05). CONCLUSION: Polymorphisms of rs662799 and rs2266788 in APOA5 gene, rs320 in LPL gene and rs708272 in CETP gene had significant association with the effect of the lipid-lowering therapy via atorvastatin calcium on ischemic stroke patients. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27415775

[12] Regulation of Hepatic Triacylglycerol Metabolism by CGI-58 Does Not Require ATGL Co-activation. Lord CC, Ferguson D, Thomas G et al. Cell Rep 2016. Adipose triglyceride lipase (ATGL) and comparative gene identification 58 (CGI-58) are critical regulators of triacylglycerol (TAG) turnover. CGI-58 is thought to regulate TAG mobilization by stimulating the enzymatic activity of ATGL. However, it is not known whether this coactivation function of CGI-58 occurs in vivo. Moreover, the phenotype of human CGI-58 mutations suggests ATGL-independent functions. Through direct comparison of mice with single or double deficiency of CGI-58 and ATGL, we show here that CGI-58 knockdown causes hepatic steatosis in both the presence and absence of ATGL. CGI-58 also regulates hepatic diacylglycerol (DAG) and inflammation in an ATGL-independent manner. Interestingly, ATGL deficiency, but not CGI-58 deficiency, results in suppression of the hepatic and adipose de novo lipogenic program. Collectively, these findings show that CGI-58 regulates hepatic neutral lipid storage and inflammation in the genetic absence of ATGL, demonstrating that mechanisms driving TAG lipolysis in hepatocytes differ significantly from those in adipocytes. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27396333

[13] Genotype-Dependent Effects of Dalcetrapib on Cholesterol Efflux and Inflammation: Concordance with Clinical Outcomes. Tardif JC, Rhainds D, Brodeur M et al. Circulation. Cardiovascular genetics 2016. BACKGROUND: Dalcetrapib effects on cardiovascular outcomes are determined by adenylyl cyclase 9 (ADCY9) gene polymorphisms. Our aim was to determine whether these clinical endpoint results are also associated with changes in reverse cholesterol transport and inflammation. METHODS AND RESULTS: Participants of the dal-OUTCOMES and dal-PLAQUE-2 trials were randomly assigned to receive dalcetrapib or placebo in addition to standard care. High-sensitivity C-reactive protein (hs-CRP) was measured at baseline and end of study in 5243 patients from dal-OUTCOMES also genotyped for the rs1967309 polymorphism in ADCY9 Cholesterol efflux capacity of HDL from J774 macrophages following cAMP stimulation was determined at baseline and 12 months in 171 genotyped patients from dal-PLAQUE-2. Treatment with dalcetrapib resulted in placebo-adjusted geometric mean percent increases in hs-CRP from baseline to end of trial of 18.1% (p=0.0009) and 18.7% (p=0.00001) in participants with the GG and AG genotypes respectively, but change was -1.0% (p=0.89) in those with the protective AA genotype. There was an interaction between the treatment arm and the genotype groups (p=0.02). While the mean change in cholesterol efflux was similar among study arms in patients with GG genotype (mean: 7.8% and 7.4%), increases were 22.3% and 3.5% with dalcetrapib and placebo for those with AA genotype (p=0.004). There was a significant genetic effect for change in efflux for dalcetrapib (p=0.02), but not with placebo. CONCLUSIONS: Genotype-dependent effects on C-reactive protein and cholesterol efflux are supportive of dalcetrapib benefits on atherosclerotic cardiovascular

[14] Effects of Vascular and Nonvascular Adverse Events and of Extended-Release Niacin With Laropiprant on Health and Healthcare Costs. Kent S, Haynes R, Hopewell JC et al. Circulation. Cardiovascular quality and outcomes 2016.BACKGROUND: Extended-release niacin with laropiprant did not significantly reduce the risk of major vascular events and increased the risk of serious adverse events in Heart Protection Study 2-Treatment of HDL to Reduce the Incidence of Vascular Events (HPS2-THRIVE), but its net effects on health and healthcare costs are unknown. METHODS AND RESULTS: 25 673 participants aged 50 to 80 years with previous cardiovascular disease were randomized to 2 g of extended-release niacin with 40 mg of laropiprant daily versus matching placebo, in addition to effective statin-based low-density lipoprotein cholesterol-lowering treatment. The net effects of niacin-laropiprant on quality-adjusted life years and hospital care costs (2012 UK pound; converted into US $ using purchasing power parity index) during 4 years in HPS2-THRIVE were evaluated using estimates of the impact of serious adverse events on health-related quality of life and hospital care costs. During the study, participants assigned niacin-laropiprant experienced marginally but not statistically significantly lower survival (0.012 fewer years [standard error (SE) 0.007]), fewer quality-adjusted life years (0.023 [SE 0.007] fewer using UK EQ-5D scores; 0.020 [SE 0.006] fewer using US EQ-5D scores) and accrued greater hospital costs (UK pound101 [SE pound37]; US $145 [SE $53]). Stroke, heart failure, musculoskeletal events, gastrointestinal events, and infections were associated with significant decreases in health-related quality of life in both the year of the event and in subsequent years. All serious vascular and nonvascular events were associated with substantial increases in hospital care costs. CONCLUSIONS: In HPS2-THRIVE, the addition of extended-release niacin-laropiprant to statin-based therapy reduced quality of life-adjusted survival and increased hospital costs. CLINICAL TRIAL REGISTRATION: URL: http://clinicaltrials.gov/. Unique identifier: NCT00461630. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27407053


[16] Clinical Trial of the Protein Farnesylation Inhibitors Lonafarnib, Pravastatin, and Zoledronic Acid in Children With Hutchinson-Gilford Progeria Syndrome. Gordon LB, Kleinman ME, Massaro J et al. Circulation 2016; 134:114-125. BACKGROUND: Hutchinson-Gilford progeria syndrome is an extremely rare, fatal, segmental premature aging syndrome caused by a mutation in LMNA yielding the farnesylated aberrant protein progerin. Without progerin-specific treatment, death occurs at an average age of 14.6 years from an accelerated atherosclerosis. A previous single-arm clinical trial demonstrated that the protein farnesyltransferase inhibitor lonafarnib ameliorates some aspects of cardiovascular and bone
disease. This present trial sought to further improve disease by additionally inhibiting progerin prenylation. METHODS: Thirty-seven participants with Hutchinson-Gilford progeria syndrome received pravastatin, zoledronic acid, and lonafarnib. This combination therapy was evaluated, in addition to descriptive comparisons with the prior lonafarnib monotherapy trial. RESULTS: No participants withdrew because of side effects. Primary outcome success was predefined by improved per-patient rate of weight gain or carotid artery echodensity; 71.0% of participants succeeded (P<0.0001). Key cardiovascular and skeletal secondary variables were predefined. Secondary improvements included increased areal (P=0.001) and volumetric (P<0.001-0.006) bone mineral density and 1.5- to 1.8-fold increases in radial bone structure (P<0.001). Median carotid artery wall echodensity and carotid-femoral pulse wave velocity demonstrated no significant changes. Percentages of participants with carotid (5% to 50%; P=0.001) and femoral (0% to 12%; P=0.13) artery plaques and extraskeletal calcifications (34.4% to 65.6%; P=0.006) increased. Other than increased bone mineral density, no improvement rates exceeded those of the prior lonafarnib monotherapy treatment trial. CONCLUSIONS: Comparisons with lonafarnib monotherapy treatment reveal additional bone mineral density benefit but likely no added cardiovascular benefit with the addition of pravastatin and zoledronic acid. CLINICAL TRIAL REGISTRATION: URL: http://www.clinicaltrials.gov/. Unique identifiers: NCT00879034 and NCT00916747. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27400896

[17] Effects of atorvastatin on renal function in patients with dyslipidemia and chronic kidney disease: assessment of clinical usefulness in CKD patients with atorvastatin (ASUCA) trial. Kimura G, Kasahara M, Ueshima K et al. Clinical and experimental nephrology 2016.BACKGROUND: Dyslipidemia is a risk factor for the progression of chronic kidney disease (CKD). While conventional lipid lowering therapy provides a benefit to CKD management, the effect of statins on eGFR remains unclear. METHODS: A prospective, multi-center, open-labeled, randomized trial. Total of 349 CKD patients with hyperlipidemia were randomized into 2 groups, and followed for 2 years. Group A included patients who were treated with atorvastatin. Group C were treated with conventional lipid lowering drugs other than statin. Primary endpoint was changes in eGFR. Secondary endpoints included changes in urinary albumin excretion, serum LDL-C, serum triglyceride, cardio-vascular events and all-cause mortality. RESULTS: As the primary endpoint, eGFR decreased by 2.3 ml/min/1.73 m2 in Group A and by 2.6 ml/min/1.73 m2 in Group C, indicating that there was no difference in change of eGFR between the two groups. As secondary endpoints, atorvastatin succeeded to reduce serum LDL-C level significantly and rapidly, but conventional therapy did not. In fact, mean LDL-C level did not reach the target level of 100 mg/dl in Group C. Serum triglyceride was lowered only by atorvastatin, but not conventional drugs. The number of cardiovascular events and all-cause mortality did not differ between in two groups. CONCLUSION: The ASUCA (Assessment of Clinical Usefulness in CKD Patients with Atorvastatin) trial demonstrated that atorvastatin failed to exhibit reno-protectors compared to conventional therapy in Japanese patients with dyslipidemia and CKD. It would be due in part to the ability of atorvastatin to more potently
reduce serum LDL and triglycerides compared to conventional therapy. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27392909

[18] **Switching Lopinavir/Ritonavir to Atazanavir/Ritonavir vs Adding Atorvastatin in HIV-Infected Patients Receiving Second-Line Antiretroviral Therapy With Hypercholesterolemia: A Randomized Controlled Trial.** Wangpatharawanit P, Sungkanuparph S. *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America* 2016. A randomized controlled trial was conducted among human immunodeficiency virus-infected patients receiving lopinavir/ritonavir-based regimens with hypercholesterolemia. Reduction of total cholesterol and low-density lipoprotein was significantly greater in patients who were randomized to the addition of atorvastatin compared with those who were switched from lopinavir/ritonavir to atazanavir/ritonavir. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27402817

[19] **The Effects of Dietary Omega-3s on Muscle Composition and Quality in Older Adults.** Smith Gl. *Current nutrition reports* 2016; 5:99-105. This review will focus on findings from the few studies performed to date in humans to examine changes in muscle protein turnover, lean or muscle mass and physical function following fish oil-derived omega-3 fatty acid treatment. Although considerable gaps in our current knowledge exist, hypertrophic responses (e.g., improvements in the rate of muscle protein synthesis and mTOR signaling during increased amino acid availability and an increase in muscle volume) have been reported in older adults following prolonged (8 to 24 weeks) of omega-3 fatty acid supplementation. There is also accumulating evidence that increased omega-3 fatty acid levels in red blood cells are positively related to strength and measures of physical function. As a result, increased omega-3 fatty acid consumption may prove to be a promising low-cost dietary approach to attenuate or prevent aging associated declines in muscle mass and function. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27398264

[20] **Lipids, Statins and Heart Failure: An update.** Katsiki N, Doumas M, Mikhailidis DP. *Current pharmaceutical design* 2016.: Background: Heart failure (HF) is characterized by cardiac functional and structural alterations, progressively leading to clinical symptoms and signs. Certain neurohormonal systems (i.e. the sympathetic nervous system, the renin-angiotensin-aldosterone system and the natriuretic peptide system) as well as interactions between endothelial, monocytes/macrophages and myocardial cells are involved in the process. METHODS: The present narrative review discusses the relationships between lipids, statins and HF. RESULTS: Lipid metabolism is involved in cardiac function. Inflammation, oxidative stress, endothelial and platelet dysfunction, activation of neurohormonal systems, adverse cardiac remodeling, haemodynamic disorders and arrhythmogenesis predispose to HF development and progression. Statins have been shown to reduce HF incidence possibly via their pleiotropic actions on the above mentioned mechanisms. Other cardiovascular (CV) risk factors affecting HF prevalence and outcomes include metabolic syndrome, non-alcoholic fatty liver disease, chronic kidney disease, hyperuricaemia, epicardial fat and increased arterial stiffness that are
improved following statin therapy. CONCLUSIONS: Lipid disorders are involved in HF development and progression. Statins may beneficially affect these disorders as well as other CV risk factors linked to HF. However, the impact of statins in patients with established HF has yet to be determined. Further studies are needed to unveil potential benefits of statin therapy (or some statins) in specific groups of HF patients. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27396601

[21] Benefit-Risk Assessment of Fish Oil in Preventing Cardiovascular Disease. Lands B. Drug Saf 2016. Cardiovascular disease (CVD) is a preventable disease, which combines two general processes: chronic vascular inflammation and acute thrombosis. Both are amplified with positive feedback signals by n-6 eicosanoids derived from food-based n-6 highly unsaturated fatty acids (n-6 HUFA). This amplification is lessened by competing actions of n-3 HUFA. Death results from fatal interactions of the vascular wall with platelets and clotting proteins. The benefits of fish oil interventions are confounded by complex details in pharmacokinetics, pharmacodynamics, adverse events, timescale factors, topology, financial incentives and people's sense of cause and effect. Two basic aspects of n-3 HUFA that are overlooked in CVD dynamics are saturable, hyperbolic responses of the enzymes continually supplying n-6 HUFA and hard-to-control positive feedback receptor signals by excessive n-6 HUFA-based mediators. Multiple feedback loops in inflammation and thrombosis have diverse mediators, and reducing one mediator that occurs above its rate-limiting levels may not reduce the pathophysiology. Clinicians have developed some successful interventions that decrease CVD deaths in the form of secondary prevention. However, the current high CVD prevalence in the USA remains unchanged, and successful primary prevention of CVD remains uncertain. This review weighs the available evidence to help clinicians, the biomedical community and the public put the use of fish oil supplements into a balanced perspective. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27412006

[22] Ezetimibe-Statin Combination Therapy. Nussbaumer B, Glechner A, Kaminski-Hartenhalter A et al. Deutsches Arzteblatt international 2016; 113:445-453. BACKGROUND: To date, most clinical comparisons of ezetimibe-statin combination therapy versus statin monotherapy have relied entirely on surrogate variables. In this systematic review, we study the efficacy and safety of ezetimibe-statin combination therapy in comparison to statin monotherapy in terms of the prevention of cardiovascular events in hyperlipidemic patients with atherosclerosis and/or diabetes mellitus. METHODS: This review is based on a systematic literature search (1995 to July 2015) in PubMed, the Excerpta Medica Database (EMBASE), the Cochrane Library, and the ClinicalTrials.gov registry. RESULTS: Nine randomized, controlled trials with data from a total of 19,461 patients were included. Ezetimibe- statin combination therapy was associated with a lower risk of cardiovascular events than statin monotherapy: 33% of the patients treated with ezetimibe and a statin, and 35% of those treated with a statin alone, had a cardiovascular event within seven years (number needed to treat [NNT]: 50 over 7 years). Combination therapy was also significantly more effective in preventing a composite endpoint consisting of death due to cardiovascular disease, nonfatal myocardial infarction, unstable angina pectoris, coronary
revascularization, and nonfatal stroke (hazard ratio [HR] 0.94, 95% confidence interval [0.89; 0.99]; p = 0.016). Diabetic patients benefited from combination therapy rather than monotherapy with respect to cardiovascular morbidity (HR 0.87 [0.78; 0.94]). On the other hand, the addition of ezetimibe to statin therapy did not lessen either cardiovascular or overall mortality. Serious undesired events occurred in 38% of the patients taking ezetimibe and a statin and in 39% of the patients taking a statin alone (relative risk 1.09 [0.77; 1.55]).

CONCLUSION: In high-risk patients with an acute coronary syndrome, combination therapy with ezetimibe and a statin lowered the risk of cardiovascular events in comparison to statin monotherapy. The risk of dying or suffering an adverse drug effect was similar in the two treatment groups. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27412989

[23] Jiang Tang Xiao Ke Granule, a Classic Chinese Herbal Formula, Improves the Effect of Metformin on Lipid and Glucose Metabolism in Diabetic Mice. Zhang Y, An H, Pan SY et al. Evidence-based complementary and alternative medicine : eCAM 2016; 2016:1592731. In the present study, the hypoglycemic, hypolipidemic, and antioxidative effects of metformin (MET) combined with Jiang Tang Xiao Ke (JTXK) granule derived from the "Di Huang Tang" were evaluated in mice with type 2 diabetes mellitus (DM) induced by high-fat diet/streptozotocin. DM mice were orally treated with MET (0.19 g/kg) either alone or combined with different doses (1.75, 3.5, or 7 g/kg) of JTXK for 4 weeks. Results showed that the serum and hepatic glucose, lipids, and oxidative stress levels were elevated in DM mice, when compared with the normal mice. MET treatment decreased FBG and serum glucagon levels of DM mice. Combination treatment with MET and JTXK 3.5 g/kg increased the hypoglycemia and insulin sensitivity at 4 weeks when compared with the DM mice treated with MET alone. However, neither MET nor MET/JTXK treatment could completely reverse the hyperglycemia in DM mice. JTXK enhanced the serum triglyceride (TG) and hepatic lipid-lowering effect of MET in a dose-dependent manner in DM mice. JTXK 1.75 and 3.5 g/kg improved the hepatoprotective effect of MET in DM mice. Synergistic effect of combination treatment with MET and JTXK on antioxidant stress was also found in DM mice compared with MET alone. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27418937

[24] Autoimmune-like drug-induced liver injury: a review and update for the clinician. Stine JG, Northup PG. Expert opinion on drug metabolism & toxicology 2016. INTRODUCTION: Autoimmune-like drug-induced liver injury (DI-AIH) is a rare but serious event with a growing body of scientific evidence and a fair degree of uncertainty. AREAS COVERED: This review covers the definition, pathophysiology, treatment and patient-centered outcomes of DI-AIH and presents up-to-date information on the most commonly implicated drugs. EXPERT OPINION: A high degree of clinical suspicion is required for the diagnosis of DI-AIH. This diagnosis should be considered in any patient with either acute or chronic elevations in liver-associated enzymes. Prevalence rates exceed 15% based on large international registry data. Autoantibodies, while common, are neither specific nor diagnostic of DI-AIH. Histology may be helpful in describing subtle differences between DI-AIH and de novo idiopathic autoimmune hepatitis (iAIH), but oftentimes the two are indistinguishable histologically. Alpha-methyldopa, fibrates, hydralazine,
minocycline, nitrofurantoin, HMG-CoA reductase inhibitors (statins), iplimumbab and tumor necrosis factor alpha antagonists are the most commonly associated drugs with DI-AIH. Complete recovery of liver injury is most often seen with DI-AIH, however, cases of prolonged injury may occur and may require treatment with immunosuppressive therapy for which the lowest dose over the shortest possible duration should be prescribed with a high-degree of awareness of potential side effects. Relapse following cessation of corticosteroids for suspected DI-AIH should prompt reconsideration of the diagnosis and further exploration into possible iAIH.Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27402321

[25] High-dose atorvastatin is associated with lower IGF-1 levels in patients with type 1 diabetes. Bergen K, Brismar K, Tehrani S. Growth hormone & IGF research : official journal of the Growth Hormone Research Society and the International IGF Research Society 2016; 29:78-82. INTRODUCTION: Insulin-like growth factor 1 (IGF-1) and insulin-like growth factor binding protein 1 (IGFBP-1) play an important role in vascular health. Many patients with type 1 diabetes are medicated with HMG-CoA reductase inhibitors, statins, in order to prevent vascular complications. Yet little is known about the effect of statins on the IGF-1/IGFBP-1 axis in these patients. OBJECTIVES: The aim of this study was to evaluate the effect of atorvastatin treatment on IGF-1 and IGFBP-1 with regards to microvascular function. DESIGN: Twenty patients with type 1 diabetes received either placebo or 80mg atorvastatin for two months in a double-blinded cross-over study. IGF-1 and IGFBP-1 levels were assessed before and after each treatment period. Skin microcirculation was studied using Doppler perfusion imaging during iontophoresis of acetylcholine and sodium nitroprusside to assess endothelium-dependent and endothelium-independent microvascular reactivity, respectively. RESULTS: Treatment with high-dose atorvastatin was associated with a significant decrease in IGF-1 levels compared to placebo (p<0.05, ANOVA repeated measures), whereas no effect was seen on IGFBP-1 or the IGF-1/IGFBP-1 ratio. These variables did not correlate with measurements of skin microvascular reactivity. CONCLUSIONS: The study found that treatment with high-dose atorvastatin was associated with reduced IGF-1 levels, which may indicate a potential negative effect on microvascular function and long-term risk of microangiopathy development. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27400272

[26] Hypercholesterolemia - Where are we today? Where are we going?]. Gitt AK, Zahn R. Herz 2016. Hypercholesterolemia is one of the major modifiable risk factors for the development of atherosclerosis. Increasing LDL cholesterol is associated with an increased risk of developing cardiovascular diseases as well as cardiovascular ischemic complications. Studies with statins and ultimately with ezetimibe have been able to impressively demonstrate that lowering LDL cholesterol contributes to a significant reduction of cardiovascular ischemic complications. Based on the results of randomized trials for lipid lowering, the practice guidelines developed by the professional societies have defined LDL cholesterol goals. High-risk patients, such as patients with clinically manifest cardiovascular disease, type 2 diabetes, type 1 diabetes with organ damage, moderate or severe chronic kidney disease or a risk of SCORE >/=10 %, should reach LDL cholesterol values <70 mg/dl. Data from observational trials
demonstrated that in daily practice only about 20% of treated high-risk patients reached this recommended LDL cholesterol goal. The therapeutic options are not yet exhausted; patients are treated mainly with low or at most average statin dosages. There should be more potent and high-dose statins used as well as the combination therapy of statin and ezetimibe to achieve the recommended LDL cholesterol goals. Specific cardiac rehabilitation and prevention programs with regular benchmarking could support improved goal-achievement. The new therapeutic option of PCSK9 inhibitors, which significantly and safely lower LDL cholesterol on top of statins and ezetimibe, is currently investigated in large randomized outcome trials. PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27412663

AIM: To investigate whether switching to high-dose rosuvastatin, add-on statin nicotinic acid or add-on statin fenofibrate would alter 25(OH)VitD levels in patients with mixed dyslipidemia who are already on a conventional statin dose. METHODS: This is a prespecified analysis of a previously published study. Forty-four patients with mixed dyslipidemia not at treatment goal despite treatment with simvastatin 10-40 mg or atorvastatin 10-20 mg or rosuvastatin 5-10 mg were randomly allocated to switch to rosuvastatin 40 mg (n=17), add-on statin extended release nicotinic acid (ER-NA)/laropiprant (LRPT) (1000/20 mg first four weeks and 2000/40 mg thereafter) (n=14), or add-on statin micronized fenofibrate (200 mg) for three months. The endpoint for this analysis was between-group difference in changes in 25(OH)VitD levels.
RESULTS: Serum 25(OH)VitD levels did not significantly change in any group. In the switch to the highest dose of rosuvastatin group and the add-on statin ER-NA/LRPT group there was an insignificant decrease in 25(OH)VitD levels [-4.7% [from 16.8 (3.2-37) to 16.0 (7.9-51.6)] and -14.8% [from 12.8 (2.0-54.8) to 10.9 (2.4-34)], respectively], while in the add-on statin fenofibrate group there was an insignificant increase [+13% (from 14.5 (1.0-42) to 16.4 (4.4-30.4) ng/mL)]. No significant difference between groups was found. CONCLUSION: In patients already on a conventional statin dose, neither switching to high-dose rosuvastatin (40 mg) nor add-on statin ER-NA/LRPT or fenofibrate were associated with significant changes in 25(OH)VitD serum levels. Hippokratia 2015; 19 (2):136-140. PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27418762

[28] Lipid mediators as regulators of human ILC2 function in allergic diseases. Konya V, Mjosberg J. Immunology letters 2016. Group 2 innate lymphoid cells (ILC2) are specialized in type 2 immunity. ILC2 are activated early in immune responses and, despite their low abundance, are able to initiate and amplify allergic inflammation by orchestrating other type 2 immune cells. Based on recent discoveries, the spectrum of ILC2 regulating factors has been extended. It is now well established that not only epithelial cell-derived innate cytokines, but also bioactive lipids can regulate ILC2 activity and accumulation. Additionally, ILC2 appear to be
susceptible to changes in the cytokine milieu and can acquire an ILC1-like phenotype due to a high degree of cellular plasticity. As ILC2 are fundamentally involved in the pathogenesis of type 2 diseases, they represent a promising therapeutic target for allergic airway and skin diseases. In this review we summarize the current knowledge about ILC2 biology in the allergy context, with a particular focus on the emerging role of lipid mediators in regulating ILC2 function. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27396531

[29] Charge effect of a liposomal delivery system encapsulating simvastatin to treat experimental ischemic stroke in rats. Campos-Martorell M, Cano-Sarabia M, Simats A et al. International journal of nanomedicine 2016; 11:3035-3048.BACKGROUND AND AIMS: Although the beneficial effects of statins on stroke have been widely demonstrated both in experimental studies and in clinical trials, the aim of this study is to prepare and characterize a new liposomal delivery system that encapsulates simvastatin to improve its delivery into the brain. MATERIALS AND METHODS: In order to select the optimal liposome lipid composition with the highest capacity to reach the brain, male Wistar rats were submitted to sham or transitory middle cerebral arterial occlusion (MCAO) surgery and treated (intravenous [IV]) with fluorescent-labeled liposomes with different net surface charges. Ninety minutes after the administration of liposomes, the brain, blood, liver, lungs, spleen, and kidneys were evaluated ex vivo using the Xenogen IVIS((R)) Spectrum imaging system to detect the load of fluorescent liposomes. In a second substudy, simvastatin was assessed upon reaching the brain, comparing free and encapsulated simvastatin (IV) administration. For this purpose, simvastatin levels in brain homogenates from sham or MCAO rats at 2 hours or 4 hours after receiving the treatment were detected through ultra-high-protein liquid chromatography. RESULTS: Whereas positively charged liposomes were not detected in brain or plasma 90 minutes after their administration, neutral and negatively charged liposomes were able to reach the brain and accumulate specifically in the infarcted area. Moreover, neutral liposomes exhibited higher bioavailability in plasma 4 hours after being administered. The detection of simvastatin by ultra-high-protein liquid chromatography confirmed its ability to cross the blood-brain barrier, when administered either as a free drug or encapsulated into liposomes. CONCLUSION: This study confirms that liposome charge is critical to promote its accumulation in the brain infarct after MCAO. Furthermore, simvastatin can be delivered after being encapsulated. Thus, simvastatin encapsulation might be a promising strategy to ensure that the drug reaches the brain, while increasing its bioavailability and reducing possible side effects. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27418824

[30] Statins in Familial Hypercholesterolemia: Consequences for Coronary Artery Disease and All-Cause Mortality. Besseling J, Hovingh GK, Huijgen R et al. Journal of the American College of Cardiology 2016; 68:252-260.BACKGROUND: A statin-induced reduction of coronary artery disease (CAD) events and mortality has not been adequately quantified in patients with heterozygous familial hypercholesterolemia (FH). OBJECTIVES: This study estimated the relative risk reduction for CAD and mortality by statins in heterozygous FH patients. METHODS: The authors included all adult heterozygous FH patients, identified by the Dutch screening program.
for FH between 1994 and 2013, who were free of CAD at baseline. Hospital, pharmacy, and mortality records between 1995 and 2015 were linked to these patients. The primary outcome was the composite of myocardial infarction, coronary revascularization, and death from any cause. The effect of statins (time-varying) was determined using a Cox proportional hazard model, while correcting for the use of other lipid-lowering therapy, thrombocyte aggregation inhibitors, and antihypertensive and antidiabetic medication. The authors applied inverse-probability-for-treatment weighting (IPTW) to account for differences at baseline between statin users and never-users. RESULTS: The authors obtained medical records of 2,447 patients, of whom 888 were excluded on the basis of age <18 years or previous CAD. Simvastatin 40 mg and atorvastatin 40 mg accounted for 23.1% and 22.8% of all prescriptions, respectively. Statin users (n = 1,041) experienced 89 CAD events and 17 deaths during 11,674 person-years of follow-up versus statin never-users (n = 518), who had 89 CAD events and 17 deaths during 4,892 person-years (combined rates 8.8 vs. 5.3 per 1,000 person-years, respectively; p < 0.001). After applying IPTW and adjusting for other medications, the hazard ratio of statin use for CAD and all-cause mortality was 0.56 (95% confidence interval: 0.33 to 0.96). CONCLUSIONS: In patients with heterozygous FH, moderate- to high-intensity statin therapy lowered the risk for CAD and mortality by 44%. This is essential information in all cost-effectiveness studies of this disorder, such as when evaluating reimbursement of new lipid-lowering therapies.


[34] Circulating N-Linked Glycoprotein Side-Chain Biomarker, Rosuvastatin Therapy, and Incident Cardiovascular Disease: An Analysis From the JUPITER Trial. Akinkuolie AO, Glynn RJ, Padmanabhan L et al. Journal of the American Heart Association 2016; 5. BACKGROUND: GlycA, a novel protein glycan biomarker of N-acetyl side chains of acute-phase proteins, was recently associated with incident cardiovascular disease (CVD) in healthy women. Whether GlycA predicts CVD events in the setting of statin therapy in men and women without CVD but with evidence of chronic inflammation is unknown. METHODS AND RESULTS: In the Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) trial (NCT00239681), participants with low-density lipoprotein cholesterol <130 mg/dL and high-sensitivity C-reactive protein (hsCRP) >/=2 mg/L were randomized to rosuvastatin 20 mg/day or placebo. GlycA was quantified by nuclear magnetic resonance spectroscopy in 12,527 before
randomization and 10,039 participants at 1 year. A total of 310 first primary CVD events occurred during maximum follow-up of 5.0 years (median, 1.9). GlycA increased minimally after 1 year on study treatment: 6.8% and 4.7% decrease in the rosvuatin and placebo groups, respectively. Overall, baseline GlycA levels were associated with increased risk of CVD: multivariable-adjusted hazard ratio (HR) per SD increment, 1.20 (95% CI, 1.08-1.34; P=0.0006). After additionally adjusting for hsCRP, this was slightly attenuated (HR, 1.18; 95% CI, 1.04-1.35; P=0.01). On-treatment GlycA levels were also associated with CVD; corresponding multivariable-adjusted HRs per SD before and after additionally adjusting for hsCRP: 1.27 (95% CI, 1.13-1.42; P<0.0001) and 1.24 (95% CI, 1.07-1.44; P=0.004), respectively. Tests for heterogeneity by treatment arm were not significant (P for interaction, >0.20). CONCLUSION: In the JUPITER trial, increased levels of GlycA were associated with an increased risk of CVD events independent of traditional risk factors and hsCRP. CLINICAL TRIALS REGISTRATION: URL: http://www.clinicaltrials.gov/. Unique identifier: NCT00239681.Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27413042

[35] Efficacy and Safety of Long-term Coadministration of Fenofibrate and Ezetimibe in Patients with Combined Hyperlipidemia: Results of the EFECTL Study. Oikawa N, Yamashita S, Nakaya N et al. Journal of atherosclerosis and thrombosis 2016.AIM: We investigated the safety and efficacy of a long-term combination therapy with fenofibrate and ezetimibe in Japanese patients with combined hyperlipidemia, in comparison with fenofibrate or ezetimibe alone. METHODS: The study was a three-arm parallel-group, open-label randomized trial. Eligible patients were assigned to a combination therapy with fenofibrate (200 mg/day in capsule form or 160 mg/day in tablet form) and ezetimibe (10 mg/day), the fenofibrate monotherapy, or the ezetimibe monotherapy, which lasted for 52 weeks. The changes in serum low-density lipoprotein (LDL) cholesterol and triglycerides were the primary outcomes. RESULTS: A total of 236 patients were assigned to one of the three treatments, and the number of patients included in the final analysis was 107 in the combination therapy, 52 in the fenofibrate monotherapy, and 51 in the ezetimibe monotherapy. Mean +/−SD changes in LDL cholesterol were -24.2%+/−14.7% with combination therapy, -16.0%+/−16.0% with fenofibrate alone, and -17.4%+/−10.1% with ezetimibe alone. The combination therapy resulted in a significantly greater reduction in LDL cholesterol as compared with each monotherapy (p0.01 for each). The corresponding values for triglycerides were -40.0%+/−29.5%, -40.1%+/−28.7%, and -3.4%+/−32.6%, respectively. Fenofibrate use was associated with some changes in laboratory measurements, but there was no differential adverse effect between the combination therapy and fenofibrate monotherapy. CONCLUSION: The combination therapy with fenofibrate and ezetimibe substantially reduces concentrations of LDL cholesterol and triglycerides and is safe in a long-term treatment in Japanese patients with combined hyperlipidemia.Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27397061

[36] In Vitro Assays for the Discovery of PCSK9 Autoprocessing Inhibitors. Salowe SP, Zhang L, Zokian HJ et al. Journal of biomolecular screening 2016.PCSK9 plays a significant role in regulating low-density lipoprotein (LDL) cholesterol levels and has become an important drug
target for treating hypercholesterolemia. Although a member of the serine protease family, PCSK9 only catalyzes a single reaction, the autocleavage of its prodomain. The maturation of the proprotease is an essential prerequisite for the secretion of PCSK9 to the extracellular space where it binds the LDL receptor and targets it for degradation. We have found that a construct of proPCSK9 where the C-terminal domain has been truncated has sufficient stability to be expressed and purified from Escherichia coli for in vitro study of autoprocessing. Using automated Western analysis, we demonstrate that autoprocessing exhibits the anticipated first-order kinetics. A high-throughput time-resolved fluorescence resonance energy transfer assay for autocleavage has been developed using a PCSK9 monoclonal antibody that is sensitive to the conformational changes that occur upon maturation of the proprotease. Kinetic theory has been developed that describes the behavior of both reversible and irreversible inhibitors of autocleavage. The analysis of an irreversible lactone inhibitor validates the expected relationship between potency and the reaction end point. An orthogonal liquid chromatography-mass spectrometry assay has also been implemented for the confirmation of hits from the antibody-based assays.

[37] **Type 1 Hyperlipoproteinemia due to Compound Heterozygous Rare Variants in GCKR.**
Shetty S, Xing C, Garg A. *The Journal of clinical endocrinology and metabolism* 2016:jc20162179.BACKGROUND: Type 1 hyperlipoproteinemia (T1HLP) is a rare, autosomal recessive disorder characterized by extreme elevations in serum triglyceride (TG) levels. Despite considerable progress in identifying several causal genes for T1HLP such as, LPL, APOC2, APOA5, LMF1 and GPIHBP1, the molecular basis of some extremely rare patients presenting with T1HLP remains obscure. CASE DESCRIPTION: We report a 58-year-old Hispanic female who initially presented with serum TG of 4740 mg/dL at age 23 when she was 3 weeks post-partum and was taking an oral contraceptive for two weeks. Over a period of 35 years, she has had recurrent episodes of extreme hypertriglyceridemia (fasting serum TG exceeding 2000 mg/dL), which responded to a reduction of dietary fat, fibrates and fish oil therapy. Sanger sequencing of the known T1HLP genes in this patient did not reveal any disease-causing mutations. Whole exome sequencing revealed compound heterozygous rare variants (p.Val103Met and p.Arg540Gln) in glucokinase (hexokinase 4) regulator (GCKR) gene. CONCLUSIONS: GCKR encodes glucokinase regulatory protein, which is an inhibitor of glucokinase, an enzyme that drives glucose uptake in the liver. Loss of function GCKR variants by enhancing glucose uptake in hepatocytes, may induce de novo lipogenesis and TG biosynthesis resulting in extreme hypertriglyceridemia. We conclude that compound heterozygous rare variants in GCKR cause an extremely rare unique T1HLP, most likely by inducing excessive hepatic lipogenesis.

[38] **Preoperative statin use is not associated with improvement in survival after glioblastoma surgery.** Bhavasar S, Hagan K, Arunkumar R et al. *Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia* 2016. Cohort studies have suggested that the use of statins is associated with decreased risk of glioma formation and mortality. Here, a cohort of
patients with glioblastoma multiforme (GBM) was analyzed to further investigate associations between preoperative use of statins and recurrence, and progression free and overall survival. Patients who had surgery for GBM (N=284) were followed up for a median of 18.1 months. Seventy-eight patients were taking statins preoperatively while the rest were not. Cox proportional hazards models adjusted for several covariates of interest were applied before and after propensity score matching. Compared with statin users, those not taking the lipid-lowering drugs had similar progression free survival before (hazard ratio [HR] 0.94, 95% confidence interval [CI] 0.70-1.26; p=0.68) and after propensity score matching (HR 0.95, 95% CI 0.67-1.35; p=0.68). Mortality was similar between both groups of patients before (HR 0.94, 95% CI 0.70-1.22; p= 0.73) and after propensity score matching (HR 1.13, 95% CI 0.78-1.64; p=0.49).

Age and dexamethasone use were independent prognostic factors of survival. Contrary to previously published evidence, this study could not find an association between preoperative statin use and longer survival in GBM patients. Due to the small number of patients and retrospective nature of the study, further work is needed to understand the role of perioperative statins in GBM patients.


BACKGROUND: Pro-protein convertase subtilisin/kexin type 9 (PCSK9) is a secreted protein that influences plasma levels of low-density lipoprotein cholesterol (LDL-C). Both oxidized LDL and tissue factor (TF) contributed to the development of prothrombotic state. The present study aims to explore the relationship between plasma level of PCSK9 and that of TF in patient with coronary artery disease (CAD).

METHODS: From July 2013 to March 2014, we enrolled 197 consecutive patients who underwent coronary angiography because of suspected CAD at Beijing Anzhen Hospital in this study. All patients had no history of using lipid-lowering medication. Of these 197 patients (131 male and 66 female, mean age 56.9 +/- 11.8 years), 81 had angiographically diagnosed CAD. Clinical data were collected. Plasma PCSK9 and TF were measured using enzyme-linked immunosorbent assay (ELISA). Levels of plasma PCSK9 and TF were compared and their correlation analyzed among different patient groups. RESULTS: Both plasma levels of PCSK9 (279.8 +/- 60.4 microg/L vs. 216.5 +/- 45.3 microg/L, P < 0.01) and TF (156.4 +/- 26.6 microg/mL vs. 112.1 +/- 38.3 microg/L, P < 0.01) were significantly higher in patients with CAD, as compared with those without CAD. Correlation analysis showed plasma level of PCSK9 was significantly correlated with that of TF in both patients with and without CAD. However, multivariate regression analysis after adjustment for age, gender, smoking, alcohol, hypertension and hyperlipidemia showed that only in CAD patients with type 2 diabetes mellitus, there was significant positive correlation between plasma levels of PCSK9 and TF (beta = 0.353, P < 0.01). CONCLUSIONS: The plasma level of PCSK9 is independently and positively associated with that of TF in CAD patients with diabetes mellitus, but not in those without.
diabetes mellitus. Further study is needed to investigate the underlying mechanism. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27403140

[40] The pathophysiological role of oxidized cholesterols in epicardial fat accumulation and cardiac dysfunction: a study in swine fed a high caloric diet with an inhibitor of intestinal cholesterol absorption, ezetimibe. Shimabukuro M, Okawa C, Yamada H et al. The Journal of nutritional biochemistry 2016; 35:66-73. Oxidized cholesterols (oxycholesterols) in food have been recognized as strong atherogenic components, but their tissue distributions and roles in cardiovascular diseases remain unclear. To investigate whether accumulation of oxycholesterols is linked to cardiac morphology and function, and whether reduction of oxycholesterols can improve cardiac performance, domestic male swine were randomized to a control diet (C), high caloric diet (HCD) or HCD+Ezetimibe, an inhibitor of intestinal cholesterol absorption, group (HCD+E) and evaluated for: (1) distribution of oxycholesterol components in serum and tissues, (2) levels of oxycholesterol-related enzymes, (3) paracardial and epicardial coronary fat thickness, and (4) cardiac performance. Ezetimibe treatment for 8 weeks attenuated increases in oxycholesters in the HCD group almost completely in liver, but reduced only levels of 4beta-hydroxycholesterol in left ventricular (LV) myocardium. Ezetimibe treatment altered the expression of genes for cholesterol and fatty acid metabolism and decreased the expression of CYP3A46, which catabolizes cholesterol to 4beta-hydroxycholesterol, strongly in liver. An increase in epicardial fat thickness and impaired cardiac performance in the HCD group were improved by ezetimibe treatment, and the improvement was closely related to the reduction in levels of 4beta-hydroxycholesterol in LV myocardium. In conclusion, an increase in oxycholesters in the HCD group was closely related to cardiac hypertrophy and dysfunction, as well as an increase in epicardial fat thickness. Ezetimibe may directly reduce oxycholesterol in liver and LV myocardium, and improve cardiac morphology and function. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27416363

[41] Addition of aspirin to a fish oil-rich diet decreases inflammation and atherosclerosis in ApoE-null mice. Sorokin AV, Yang ZH, Vaisman BL et al. The Journal of nutritional biochemistry 2016; 35:58-65. Aspirin (ASA) is known to alter the production of potent inflammatory lipid mediators, but whether it interacts with omega-3 fatty acids (FAs) from fish oil to affect atherosclerosis has not been determined. The goal was to investigate the impact of a fish oil-enriched diet alone and in combination with ASA on the production of lipid mediators and atherosclerosis. ApoE/-/- female mice were fed for 13 weeks one of the four following diets: omega-3 FA deficient (OD), omega-3 FA rich (OR) (1.8g omega-3 FAs/kg diet per day), omega-3 FA rich plus ASA (ORA) (0.1g ASA/kg diet per day) or an omega-3 FA deficient plus ASA (ODA) with supplement levels equivalent to human doses. Plasma lipids, atherosclerosis, markers of inflammation, hepatic gene expression and aortic lipid mediators were determined. Hepatic omega-3 FAs were markedly higher in OR (9.9-fold) and ORA (7-fold) groups. Mice in both OR and ORA groups had 40% less plasma cholesterol in very low-density lipoprotein-cholesterol and low-density lipoprotein fractions, but aortic plaque area formation was only significantly lower in the ORA group (5.5%) compared to the OD group (2.5%). Plasma PCSK9 protein levels
were approximately 70% lower in the OR and ORA groups. Proinflammatory aortic lipid mediators were 50%-70% lower in the ODA group than in the OD group and more than 50% lower in the ORA group. In summary, less aortic plaque lesions and aortic proinflammatory lipid mediators were observed in mice on the fish oil diet plus ASA vs. just the fish oil diet.

[42] Statins and Exercise Training Response in Heart Failure Patients: Insights From HF-ACTION. Kelly JP, Dunning A, Schulte PJ et al. JACC. Heart failure 2016.OBJECTIVES: The aim of this study was to assess for a treatment interaction between statin use and exercise training (ET) response. BACKGROUND: Recent data suggest that statins may attenuate ET response, but limited data exist in patients with heart failure (HF). METHODS: HF-ACTION (Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training) was a randomized trial of 2,331 patients with chronic HF with ejection fraction <=35% who were randomized to usual care or without ET. We evaluated whether there was a treatment interaction between statins and ET response for the change in quality of life and aerobic capacity (peak oxygen consumption and 6-min walk distance) from baseline to 3 months. We also assessed for a treatment interaction among atorvastatin, simvastatin, and pravastatin and change in these endpoints with ET. Multiple linear regression analyses were performed for each endpoint, adjusting for baseline covariates. RESULTS: Of 2,331 patients in the HF-ACTION trial, 1,353 (58%) were prescribed statins at baseline. Patients treated with statins were more likely to be older men with ischemic HF etiology but had similar use of renin angiotensin system blockers and beta-blockers. There was no evidence of a treatment interaction between statin use and ET on changes in quality of life or exercise capacity, nor was there evidence of differential association between statin type and ET response for these endpoints (all p values >0.05). CONCLUSIONS: In a large chronic HF cohort, there was no evidence of a treatment interaction between statin use and short-term change in aerobic capacity and quality of life with ET. These findings contrast with recent reports of an attenuation in ET response with statins in a different population, highlighting the need for future prospective studies. (Exercise Training Program to Improve Clinical Outcomes in Individuals With Congestive Heart Failure; NCT00047437).Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27395348

[43] Effects of extended-release niacin/laropiprant on correlations between apolipoprotein B, LDL-cholesterol and non-HDL-cholesterol in patients with type 2 diabetes. Brinton EA, Triscari J, Brudi P et al. Lipids in health and disease 2016; 15:116.BACKGROUND: LDL-C, non-HDL-C and ApoB levels are inter-correlated and all predict risk of atherosclerotic cardiovascular disease (ASCVD) in patients with type 2 diabetes mellitus (T2DM) and/or high TG. These levels are lowered by extended-release niacin (ERN), and changes in the ratios of these levels may affect ASCVD risk. This analysis examined the effects of extended-release niacin/laropiprant (ERN/LRPT) on the relationships between apoB:LDL-C and apoB:non-HDL-C in patients with T2DM. METHODS: T2DM patients (n = 796) had LDL-C >=1.55 and <2.97 mmol/L and TG <5.65 mmol/L following a 4-week, lipid-modifying run-in (~78 % taking statins). ApoB:LDL-C and apoB:non-HDL-C correlations were assessed after randomized (4:3), double-blind ERN/LRPT or
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placebo for 12 weeks. Pearson correlation coefficients between apoB:LDL-C and apoB:non-HDL-C were computed and simple linear regression models were fitted for apoB:LDL-C and apoB:non-HDL-C at baseline and Week 12, and the correlations between measured apoB and measured vs predicted values of LDL-C and non-HDL-C were studied. RESULTS: LDL-C and especially non-HDL-C were well correlated with apoB at baseline, and treatment with ERN/LRPT increased these correlations, especially between LDL-C and apoB. Despite the tighter correlations, many patients who achieved non-HDL-C goal, and especially LDL-C goal, remained above apoB goal. There was a trend towards greater increases in these correlations in the higher TG subgroup, non-significant possibly due to the small number of subjects. CONCLUSIONS: ERN/LRPT treatment increased association of apoB with LDL-C and non-HDL-C in patients with T2DM. Lowering LDL-C, non-HDL-C and apoB with niacin has the potential to reduce coronary risk in patients with T2DM. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27405296

[45] Antagonistic effect of atorvastatin on high fat diet induced survival during acute Chagas disease. Zhao D, Lizardo K, Cui MH et al. Microbes and infection / Institut Pasteur 2016. Chagas cardiomyopathy, which is seen in Chagas disease, is the most severe and life-threatening manifestation of infection by the kinetoplastid Trypanosoma cruzi. Adipose tissue and diet play a major role in maintaining lipid homeostasis and regulating cardiac pathogenesis during the development of Chagas cardiomyopathy. We have previously reported that T. cruzi has a high affinity for lipoproteins and that the invasion rate of this parasite increases in the presence of cholesterol, suggesting that drugs that inhibit cholesterol synthesis, such as statins, could affect infection and the development of Chagas cardiomyopathy. The dual epidemic of diabetes and obesity in Latin America, the endemic regions for Chagas disease, has led to many patients in the endemic region of infection having hyperlipidemia that is being treated with statins such as atorvastatin. The current study was performed to examine using mice fed on either regular or high fat diet the effect of atorvastatin on T. cruzi infection-induced myocarditis and to evaluate the effect of this treatment during infection on adipose tissue physiology and cardiac pathology. Atorvastatin was found to regulate lipolysis and cardiac lipidopathy during acute T. cruzi infection in mice and to enhance tissue parasite load, cardiac LDL levels, inflammation, and mortality in during acute infection. Overall, these data suggest that statins, such as atorvastatin, have deleterious effects during acute Chagas disease. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27416748

[46] Simvastatin Therapy in the Acute Stage of Traumatic Brain Injury Attenuates Brain Trauma-Induced Depression-Like Behavior in Rats by Reducing Neuroinflammation in the Hippocampus. Lim SW, Shiu CL, Liao JC et al. Neurocritical care 2016. BACKGROUND: The antidepressant-like effects of simvastatin on traumatic brain injury (TBI) remain unclear. The present study aimed to investigate the neuroprotective effects of simvastatin and determine
whether simvastatin attenuates TBI-induced depression-like behavior and, more specifically, acts as an antineuroinflammatory. METHODS: Anesthetized male Sprague-Dawley rats were divided into five groups: sham-operated controls, TBI controls, and TBI treatment with simvastatin 4, 10, or 20 mg/kg. Simvastatin was intraperitoneally injected 0, 24, and 48 h after TBI. The motor function was measured using an inclined plane, and depression-like behavior was evaluated using forced swimming tests. Neuronal apoptosis (markers: NeuN, TUNEL, caspase-3), microglia (marker: OX42) and astrocyte (marker: GFAP) activation, and TNF-alpha expression in the microglia and astrocytes of the hippocampal CA3 area were investigated using immunofluorescence assay. All parameters were measured on the 4th, 8th, and 15th day after TBI. RESULTS: TBI-induced depression-like behavior, which increased duration of immobility, was significantly attenuated by 20 mg simvastatin therapy on day 15 after TBI. TBI-induced neuronal apoptosis, microglia and astrocyte activation, and TNF-alpha expression in the microglia and astrocytes of the CA3 area of the hippocampus were significantly reduced by simvastatin treatment, particularly when 20 mg/kg was administered for 3 days. CONCLUSIONS: Intraperitoneal injection of simvastatin attenuated TBI in rats during the acute stage by reducing neuronal apoptosis, microglia, and TNF-alpha expression, thereby resulting in a reduction of depressive-like behavior. Our results suggest that simvastatin may be a promising treatment for TBI-induced depression-like behavior. PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27406816

Coutinho JM, Derkatch S, Potvin AR et al. Neurology 2016.OBJECTIVE: To determine whether large (>3 mm thick) but nonstenotic (<50%) carotid artery atherosclerotic plaque predominantly occurs ipsilateral rather than contralateral to cryptogenic stroke. METHODS: This was a cross-sectional observational study. Using a stroke registry, we identified consecutive patients with anterior circulation embolic stroke of undetermined source (ESUS). Using CT angiography, we measured carotid plaque size (thickness, mm) and carotid artery stenosis (North American Symptomatic Carotid Endarterectomy Trial method) for each patient. We dichotomized plaque size at several predefined thresholds and calculated the frequency of plaque size above each threshold ipsilateral vs contralateral to stroke. RESULTS: We included 85 patients with ESUS. Plaque with thickness >5 mm was present ipsilateral to stroke in 11% of patients, and contralateral in 1% (9/85 vs 1/85; p = 0.008). Plaque with thickness >4 mm was present ipsilateral to stroke in 19% of patients, and contralateral in 5% (16/85 vs 4/85; p = 0.002). Plaque with thickness >3 mm was present ipsilateral to stroke in 35% of patients, and contralateral in 15% (30/85 vs 13/85; p = 0.001). There was no difference in percentage stenosis ipsilateral vs contralateral to stroke (p = 0.98), and weak correlation between plaque size and stenosis (R2 = 0.26, p < 0.001). CONCLUSIONS: Large but nonstenotic carotid artery plaque is considerably more common ipsilateral than contralateral to cryptogenic stroke, suggesting that nonstenotic plaque is an underrecognized cause of stroke. We measured plaque size using CT angiography, a method that could be easily implemented in clinical practice. PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27412144
[48] Multimodal Endovascular Endoscopy in Carotid Atherosclerotic Disease. Savastano LE, Smith A, Vega K *et al.* Neurosurgery 2016; 63 Suppl 1:146. INTRODUCTION: Disruption of vulnerable atherosclerotic plaque is the precipitating factor that culminates in thrombosis and ischemia. Current technologies do not have sufficient power to identify subtle thrombogenic lesions (ie, ulcers) in the arterial endoluminal surfaces nor reliably predict markers for future symptomatology. We developed an ultra-thin scanning fiber endoscope (SFE) to directly visualize the endoluminal surface of carotid arteries and identify structural, chemical, and biological markers of vulnerable and complicated atherosclerotic plaques. METHODS: 1.2 mm and 2.1 mm endoscopes containing single optical fiber scanned by a piezoelectric drive mechanism were developed to illuminate tissue surfaces with red, blue, and green laser beams (RBG). Laser-induced backscattering (reflectance) and tissue fluorescence collected by a ring of optical fibers were then digitalized to reconstruct color videos with large fields of view. Then, SFE was studied ex vivo in human carotid arteries and in vivo in a rabbit model of atherosclerosis. After imaging, specimens were processed for histology; lesions were independently reviewed by 2 pathologists and matched to endoscopic images with analysis of variance. RESULTS: High-definition structural and chemical images of 20 carotid arteries harvested during hospital autopsies revealed 42 lesions. Based on anatomical features and tissue fluorescence, we developed a classifier that enabled identification of: healthy endovascular regions (smooth surfaces with strong homogeneous fluorescence); early plaques (dot or streak-like elevated lesions with low fluorescence); advance plaques (irregular elevated lesions with minimal to absent fluorescence); and complicated plaques (ulcers: punch-out dark-gray lesions with raised irregular bead-like borders and speckled fluorescence pattern; hematoma: absent reflection, black regions, and fluorescence). The image quality and validity of the classifier were reproduced in vivo in an atherogenic rabbit model. CONCLUSION: Multimodal SFE generates high-definition structural and label-free chemical images, and detects with high sensitivity and specificity small intravascular thrombi and subtle surface thrombogenic lesions in nonstenosing complicated plaques, even in cases not detected by conventional diagnostic modalities. Therefore, it holds the potential for becoming a new imaging platform in cerebrovascular and cardiovascular disease. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27399389

[49] Diet and Dementia, is there a Link? A Systematic Review. Ernst E. *Nutritional neuroscience* 1999; 2:1-6. The aim of this systematic review was to determine whether there is cogent and compelling evidence in the published literature for a link between dementia and nutrition. Six case control studies and 5 longitudinal investigations were included. Most of these studies were methodologically flawed. No clear association emerged between nutritional factors and dementia. There were some weak, positive but unconfirmed associations between meat consumption, intake of total fat, saturated fat and cholesterol with dementia incidence. Conversely, regular wine and fish consumption was associated with a decrease of dementia incidence, a finding which was also unconfirmed by independent data. It is concluded that, at present, no firm links have been established between nutritional factors and dementia. The few
associations that have been suggested are potentially important and should be investigated further. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27406688

[50] Effects of Fish Oil Diet and Age on the Fatty Acid Composition and the Endogenous Lipase Activity in Mouse Brain. Suzuki H, Jin Z, Wada O. *Nutritional neuroscience* 2000; 3:123-130. The influences of a fish oil diet and aging on the fatty acid composition in mouse brain, and the release of polyunsaturated fatty acids from brain membranes by endogenous lipase were studied. The changes in brain fatty acid composition with aging were determined in 5-weeks, 5-months and 19-months old mice fed on a commercial chow. Mice of different ages were also fed a fish oil or lard diet for 30 days, and the influence of the diets on brain fatty acid composition and endogenous lipase activity was analyzed. In aged mice fed on a commercial chow brain arachidonic acid and docosahexaenoic acid (%) decreased significantly, whereas blood arachidonic acid (%) increased and docosahexaenoic acid (%) did not change. The percentages of brain docosahexaenoic acid were significantly higher but those of arachidonic acid were lower in the fish oil diet group than in the lard diet group. However, there were no significant differences in the endogenous lipase activity between the different age or dietary groups. The release of arachidonic acid showed a tendency to decrease and docosahexaenoic acid to increase in mice fed on the fish oil diet. These results suggest that dietary lipids affect the percentages of arachidonic and docosahexaenoic acids which are released by the endogenous lipase in brain although the decreases in brain polyunsaturated fatty acid content with aging are not due to the enzyme activation, and dietary lipids do not influence the enzyme activity. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27416369

[51] Polyunsaturated Fatty Acids and Disease-associated and Cytokine-induced Neurological Manifestations. Turrin NP, Plata-Salaman CR. *Nutritional neuroscience* 1998; 1:395-404. Fish oil supplementation is suggested as possible mean to improve neurological manifestations of chronic diseases and cytokine immunotherapies. Preclinical and clinical studies show that fish oil supplementation seems able to reduce disease-associated anorexia and body weight loss. This improvement could be due to shifts in metabolism and changes in proinflammatory cytokine production and action. Omega-3 polyunsaturated fatty acids (PUFAs), especially eicosapentaenoic acid, are used as substrates for eicosanoid synthesis, competing for enzymes with arachidonic acid, which is a substrate for the synthesis of proinflammatory immunomodulators, such as prostaglandin E2. Fish oil supplementation is generally found to lower production of cytokines including interleukin-1 and tumor necrosis factor-alpha, thereby reducing various immune responses, including inflammation. However, conflicting results regarding the effects of fish oil interventions have been reported. The main factor that emerges from the contradictory reports is the variety of models, assays and methodologies that have been used. This brief review presents an overall perspective on the potential use of omega-3 PUFAs as a nutritional intervention to ameliorate disease-associated and cytokine-induced neurological manifestations. We conclude that substantial further research is required to understand the exact nature of n-3 PUFA-induced immunomodulation in health and disease. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27406547

[53] Single dose pharmacokinetics of atorvastatin oral formulations using a simple HPLC-UV method. Sohail M, Ahmad M, Minhas MU. Pak J Pharm Sci 2016; 29:1151-1154. The study was aimed to assess pharmacokinetics of atorvastatin (40 mg) in healthy fasted human subjects by a simple and inexpensive high performance liquid chromatography. Experimental design of the study was a randomized, two way, two periods, crossover study (single dose in fasted conditions). Eighteen (18) healthy male volunteers were enrolled according to FDA guidelines. The plasma samples were assayed using an isocratic High Performance Liquid Chromatography (HPLC) system of Agilent technologies USA consisted of an isocratic pump with column of Thermo Electron Corporation USA (ODS hypersil C 18 4.6 mm x 250 mm), a UV-visible detector set at lambdamax 237 nm. Maximum plasma concentrations (Cmax) of atorvastatin (Mean +/- SEM) for the reference product (A) found to be 13.739 +/- 0.210 ng/ml & 13.374 +/- 0.145 ng/ml for test product (B). Tmax values (Mean +/- SEM) of atorvastatin were 1.222 +/- 0.060 hours and 1.167 +/- 0.057 hours for reference and test products, respectively. The values of AUC0-oo (Mean +/- SEM) for the reference (A) and test product (B) were 73.955 +/- 1.715 ng.h/ml and 77.773 +/- 1.858 ng.h/ml, respectively. Other pharmacokinetic parameters of both products were also determined. A statistical non-significant difference between pharmacokinetic parameters has been found and both brands of atorvastatin showed the same rate and extent of absorption in healthy fasted human volunteers after single dose. A simple and cost effective HPLC method was developed and applied. PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27393428

[54] The Role of Diet, Exercise, and Medication in Blood Lipid Management of Cardiac Patients. Superko HR, Franklin BA. The Physician and sportsmedicine 1988; 16:64-81. In brief: Results of clinical investigations clearly indicate that aggressive management of blood lipids and lipoproteins can significantly benefit cardiovascular health. This finding is particularly important for patients with diagnosed coronary heart disease and those at risk for developing it. Therapy comprises reduction of excess body fat, a diet low in cholesterol and saturated fats, endurance exercise, and medication. Drugs that affect blood lipid levels include beta-blockers, bile acid binding resins, fibrin acid derivatives, hydroxymethylglutaryl-coenzyme A reductase inhibitors, nicotinic acid, and probucol. These can be used singly or in combination to bring about the desired lipid profile. PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27415991
[55] Pitavastatin Differentially Modulates MicroRNA-Associated Cholesterol Transport Proteins in Macrophages. Zhang H, Lamon BD, Moran G et al. *PloS one* 2016; 11:e0159130. There is emerging evidence identifying microRNAs (miRNAs) as mediators of statin-induced cholesterol efflux, notably through the ATP-binding cassette transporter A1 (ABCA1) in macrophages. The objective of this study was to assess the impact of an HMG-CoA reductase inhibitor, pitavastatin, on macrophage miRNAs in the presence and absence of oxidized-LDL, a hallmark of a pro-atherogenic milieu. Treatment of human THP-1 cells with pitavastatin prevented the oxLDL-mediated suppression of miR-33a, -33b and -758 mRNA in these cells, an effect which was not uniquely attributable to induction of SREBP2. Induction of ABCA1 mRNA and protein by oxLDL was inhibited (30%) by pitavastatin, while oxLDL or pitavastatin alone significantly induced and repressed ABCA1 expression, respectively. These findings are consistent with previous reports in macrophages. miRNA profiling was also performed using a miRNA array. We identified specific miRNAs which were up-regulated (122) and down-regulated (107) in THP-1 cells treated with oxLDL plus pitavastatin versus oxLDL alone, indicating distinct regulatory networks in these cells. Moreover, several of the differentially expressed miRNAs identified are functionally associated with cholesterol trafficking (six miRNAs in cells treated with oxLDL versus oxLDL plus pitavastatin). Our findings indicate that pitavastatin can differentially modulate miRNA in the presence of oxLDL; and, our results provide evidence that the net effect on cholesterol homeostasis is mediated by a network of miRNAs. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27415822

[56] [Fibrates - the present state of art]. Krysiak R, Rudzki H, Handzlik-Orlik G et al. *Polski merkuriusz lekarski : organ Polskiego Towarzystwa Lekarskiego* 2016; 40:341-344. Peroxisome proliferator-activated receptor (PPAR)alpha activators (fibrates) are one of the major group of hypolipidemic agents. Apart from lowering plasma lipid levels, fibrates produce many other favourable effects that may potentially contribute to their clinical effectiveness. Administered to patients with abnormal glucose and lipid homeostasis participating in our studies, these agents reduced monocyte and lymphocyte secretory function, systemic inflammation, hemostasis and normalized adipose tissue function and these effects did not correlate with their lipid-lowering properties. These beneficial pleiotropic effects were observed in patients with mixed dyslipidemia, isolated hypertriglyceridemia, impaired glucose tolerance, metabolic syndrome and type 2 diabetes mellitus and their strength was similar to that of statins. However, large clinical trials assessing fibrate effectiveness in the primary and secondary prevention of cardiovascular diseases provided contrasting results. In our article, we summarise the present state of knowledge on the role of fibrates in the treatment of metabolic disorders, which leads to the conclusion that fibrates are most probably efficient in primary and secondary prevention of cardiovascular diseases, particularly in patients with mixed dyslipidemia and lipid abnormalities coexisting with disorders of carbohydrate metabolism. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27403898

2016. Suboptimal adherence to statin medication is common and leads to serious negative health consequences but may respond to intervention. This review evaluated the effectiveness of interventions intended to improve adherence to statin medication. Data sources included peer-reviewed publications from Cochrane Register of Randomized Controlled Trials (RCTs), PubMed, CINAHL, and EMBase indexed between 01 October 2008 and 18 October 2015 and studies from reference lists and technical experts. RCTs that evaluated an intervention targeting adherence to self-administered statin medication for primary or secondary prevention were eligible. Two investigators independently reviewed trials, extracted data, and evaluated risk of bias. Twenty-nine RCTs reporting on 39,769 patients met inclusion. Identified RCTs exhibited methodological weaknesses: all but one failed to set inclusion parameters for medication adherence; nearly half lacked sufficient power to detect meaningful effects; and the majority had a risk of bias. Interventions were categorized into five classes (simplification of regimen, prescription cost coverage, reminders, education and information, and multi-faceted) and effects were pooled within each class. Prescription cost coverage, Hedges' g = 0.15, 95% CI [0.11:0.21], simplification of drug regimen, Hedges' g = 0.38, 95% CI [0.22:0.55], the provision of education, Hedges' g = 0.19, 95% CI [0.01:0.37], and the use of multi-faceted interventions, Hedges' g = 0.16, 95% CI [0.05:0.27], had small positive effects on statin adherence relative to usual care and reminders were promising, Hedges' g = 0.27, 95% CI [-0.05:0.60]. In conclusion, there are some successful interventions to improve adherence to statin medication but the effects are small and additional methodologically rigorous trials are needed. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27413005

[58] Comparison of serum lipid management between elderly and non-elderly patients with and without coronary heart disease (CHD). Shimizu R, Torii H, Yasuda D et al. Preventive medicine reports 2016; 4:192-198. Serum lipid management in patients aged \( \geq 75 \) has not been precisely explored. We, therefore, compared the serum lipid management between the two age groups with and without coronary heart disease (CHD). We, therefore, retrospectively reviewed medical charts of patients who were hospitalized in the departments of internal medicine during a period of 14 months. Serum lipid goal attainment was explored by applying the lipid goals for patients aged \(< 75\) to those aged \( \geq 75\). In 1988 enrolled patients, 717 subjects (36.1%) were aged \( \geq 75\). Among them, 41.3% and 32.4% of the patients had CHD, 44.2% and 41.0% were primary prevention at high-risk, and 14.5% and 14.6% were primary prevention at moderate-risk in patients aged \( \geq 75\) and aged \(< 75\), respectively. Serum LDL-C goal achievement rates in CHD were 66.9% and 65.0% in patients aged \( \geq 75\) and \(< 75\), respectively (p = 0.334). In the primary prevention at high-risk, these rates were 73.5% and 63.3%, in patients aged \( \geq 75\) and \(< 75\), respectively (p = 0.001). They were 77.9% and 58.1% in primary prevention at moderate-risk aged \( \geq 75\) and \(< 75\), respectively (p < 0.001). In CHD, lipid-lowering medication subscription rates were significantly lower in patients aged \( \geq 75\) (60.1%) than those aged \(< 75\) (73.8%, p < 0.001). In conclusion, in CHD, serum lipid goal attainment was comparable between the two age groups although the lipid-lowering drugs were less frequently prescribed in patients aged \( \geq 75\). Without CHD, it was significantly better.
in patients aged $\geq 75$ than those aged $< 75$ although the lipid-lowering drug subscription rates were comparable between the two age groups.


[59] Icosapent ethyl: Eicosapentaenoic acid concentration and triglyceride-lowering effects across clinical studies. Bays HE, Ballantyne CM, Doyle RT, Jr. et al. *Prostaglandins Other Lipid Mediat* 2016. Icosapent ethyl is a high-purity prescription form of eicosapentaenoic acid (EPA) ethyl ester approved at a dose of 4g/day as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe ($\geq 500$mg/dL) hypertriglyceridemia. This post-hoc exploratory analysis examined the relationship of icosapent ethyl dose with EPA concentrations in plasma and red blood cells (RBCs) across 3 clinical studies—a phase 1 pharmacokinetic study in healthy adult volunteers and 2 pivotal phase 3 studies (MARINE and ANCHOR) in adult patients with hypertriglyceridemia—and examined the relationship between EPA levels and TG-lowering effects in MARINE and ANCHOR. In all 3 studies, icosapent ethyl produced dose-dependent increases in the concentrations of EPA in plasma and RBCs. In both MARINE and ANCHOR, these dose-dependent EPA increases correlated with the degree of TG level lowering (all $P<0.01$). In patients with high TG levels ($\geq 200$mg/dL) and treated with icosapent ethyl 4g/day, the end-of-treatment plasma and RBC EPA concentrations were >170μg/mL and >70μg/mL, respectively. These studies support icosapent ethyl as producing predictable dose-dependent pharmacokinetics/pharmacodynamics, with TG level lowering dependent upon icosapent ethyl dose and EPA concentrations in plasma and RBCs.


[60] Low density lipoproteins and atherosclerosis—quantity or quality? Raal FJ, Areias AJ, Joffe BL. *Redox report : communications in free radical research* 1995; 1:171-176. Oxidative modification of low density lipoprotein (LDL) appears to be important in the pathogenesis of atherosclerosis. Inhibiting the oxidation of LDL may retard or prevent the atherogenic process. However, susceptibility of LDL to oxidation in vitro and its atherogenicity in vivo may not always correlate. Subjects with familial hypercholesterolaemia (FH) develop severe, premature atherosclerosis despite having large, buoyant LDL particles which are less susceptible to oxidation. High dose, long-term vitamin E increases the resistance of LDL to oxidation but, unlike probucol, has no effect on xanthoma regression in homozygous FH. In FH, the quantity of LDL takes priority and the main aim of therapy is reduction of LDL bulk. Individuals with small, dense LDL particles are at increased risk for atherosclerosis despite desirable plasma LDL cholesterol levels. Small, dense LDL particles are more susceptible to oxidation and in these subjects antioxidant therapy may be of greater benefit. In subjects with atherosclerosis, current management should be aimed primarily at reducing the LDL cholesterol level. In the future antioxidant therapy may complement our management of hypercholesterolaemia.


Current treatment of dyslipidaemia: PCSK9 inhibitors and statin intolerance. Koskinas K, Wilhelm M, Windecker S. Swiss Med Wkly 2016; 146:w14333. Statins are the cornerstone of the management of dyslipidaemias and prevention of cardiovascular disease. Although statins are, overall, safe and well tolerated, adverse events can occur and constitute an important barrier to maintaining long-term adherence to statin treatment. In patients who cannot tolerate statins, alternative treatments include switch to another statin, intermittent-dosage regimens and non-statin lipid-lowering medications. Nonetheless, a high proportion of statin-intolerant patients are unable to achieve recommended low-density lipoprotein (LDL) cholesterol goals, thereby resulting in substantial residual cardiovascular risk. Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a protease implicated in LDL receptor degradation and plays a central role in cholesterol metabolism. In recent studies, PCSK9 inhibition by means of monoclonal antibodies achieved LDL cholesterol reductions of 50% to 70% across various patient populations and background lipid-lowering therapies, while maintaining a favourable safety profile. The efficacy and safety of the monoclonal antibodies alirocumab and evolocumab were confirmed in statin-intolerant patients, indicating that PCSK9 inhibitors represent an attractive treatment option in this challenging clinical setting. PCSK9 inhibitors...
recently received regulatory approval for clinical use and may be considered in properly selected patients according to current consensus documents, including patients with statin intolerance. In this review we summarise current evidence regarding diagnostic evaluation of statin-related adverse events, particularly statin-associated muscle symptoms, and we discuss current recommendations on the management of statin-intolerant patients. In view of emerging evidence of the efficacy and safety of PCSK9 inhibitors, we further discuss the role of monoclonal PCSK9 antibodies in the management of statin-intolerant hypercholesterolaemic patients.


[64] Management of Lipid Levels and Cardiovascular Disease in HIV-Infected Individuals: Just Give Them a Statin? Stein JH. Topics in antiviral medicine 2016; 23:169-173. Current guidelines for managing cholesterol to reduce cardiovascular disease (CVD) risk focus on providing the appropriate intensity of statin therapy to reduce low-density lipoprotein cholesterol (LDL-C) level. There is very little evidence supporting the use of treatments aimed at raising high-density lipoprotein cholesterol level or reducing triglyceride levels. HIV-infected persons have excess risk of CVD compared with the general population. Statins are less effective at reducing LDL-C levels in HIV-infected persons who are also at greater risk for adverse effects from statin treatment. When selecting a statin to achieve desired lowering of LDL-C level, the potential for drug interactions with antiretroviral therapy must be considered. Information from ongoing research is expected to help identify optimal strategies for use of statin treatment in this population. This article summarizes a presentation by James H. Stein, MD, at the IAS-USA continuing education program, Improving the Management of HIV Disease, held in Chicago, Illinois, in May 201. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27398770

[65] Effect of Simvastatin on Proliferation of Vascular Smooth Muscle Cells During Delayed Cerebral Vasospasm After Subarachnoid Hemorrhage. Duan H, Zhang J, Li L, Bao S. Turkish neurosurgery 2016; 26:538-544. AIM: To explore the effect of simvastatin on proliferation of vascular smooth muscle cells (VSMCs) during delayed cerebral vasospasm (dCVS) after subarachnoid hemorrhage (SAH). MATERIAL AND METHODS: Thirty-six male New Zealand White rabbits were randomly divided into three groups: 1) Control group (n=12): given conventional breeding and normal sodium (0.9%) was injected twice into the cisterna magna. 2) SAH group (n=12): given conventional breeding and a SAH model was established. 3) Simvastatin + SAH group (n=12): given conventional breeding and simvastatin for one week, and then a SAH model was established. The first cerebral angiography was conducted before the first injection of sodium or autologous blood into the cisterna magna. The second angiography was done three days after the second injection. The ultrastructural pathology of the basilar artery was compared in three groups. The expression of platelet-derived growth factor-beta (PDGF-beta), proliferating cell nuclear antigen (PCNA) and alpha-smooth muscle
actin (alpha-SMA) in VSMCs was analysed by RT-PCR. RESULTS: Angiography examinations showed that the basilar artery was obviously contracted in the SAH group and dCVS was confirmed existence after blood injection into the cisterna magna twice. The thickness of VSMCs in the SAH group increased and the expression of PDGF-beta, PCNA, and alpha-SMA in SAH group were all increased compared to the control group (p < 0.05), and decreased while prophylactic giving simvastatin (p < 0.05). CONCLUSION: Simvastatin may relieve dCVS after SAH by inhibiting the proliferation of VSMCs. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27400100

[66] [Correlation between autophagy and polarization of macrophages in atherosclerosis plaque in arteriosclerosis obliterans amputees]. Chen WN, Guo SN, Wang JY et al. Yao xue xue bao = Acta pharmaceutica Sinica 2016; 51:68-74. This study was designed to investigate the correlation between autophagy and polarization of macrophages in atherosclerosis (AS) plaque in arteriosclerosis obliterans amputees. Femoral artery specimens from arteriosclerosis obliterans amputees were performed hematoxylin and eosin (HE) staining, oil red O and immunofluorescence staining to observe the morphology of atherosclerotic plaque, phenotype of macrophages and autophagy in plaque; using real-time quantitative RT-PCR technology to detect the mRNA level of M1 and M2 type markers in arterial tissue; to analyze polarized signal pathway and autophagy protein levels in macrophages by Western blotting. Arterial specimens staining showed obvious lipid deposition and obvious infiltration of amount of foam cells and inflammatory cells. Macrophages were mainly expression M1 type in percentage in fibrous plaque. Although both M1 and M2 macrophages were upregulated in atheromatous plaque, the increase was dominant in M2 type in percentage. The level of autophagy was significantly higher in the atheromatous plaque than that of fibrous plaque. The expression of tumor necrosis factor- alpha (TNF-alpha), monocyte chemotactic protein-1 (MCP-1), inducible nitric oxide synthase (iNOS), interleukin-6 (IL-6) and interleukin-12 (IL-12) mRNA was significantly higher in fibrous plaque than that of atheromatous plaque (P < 0.01 or 0.05), and arginase-1 (Arg-1), transforming growth factor-beta (TGF-beta), CD163 and interleukin-10 (IL-10) mRNA was significantly lower than that in atheromatous plaque (P < 0.01). The levels of p-STAT1 and NF-kappaB were significantly increased in fibrous plaque (P < 0.01), while p-STAT6 expression was significantly increased in atheromatous plaque (P < 0.01). The level of LC3-II was significantly higher in atheromatous plaque than that in fibrous plaque (P < 0.01). Macrophages in early atherosclerotic plaque were induced to M1 type through p-STAT1/NF-kappaB pathway and expressed moderate levels of autophagy; while macrophages in advanced plaques were induced to polarization of M2 type through p-STAT6 pathway. M2 macrophages expressed a higher level of autophagy than M1 macrophages. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27405164

[67] [OATP1B1 in drug-drug interactions between traditional Chinese medicine Danshensu and rosuvastatin]. Wen JH, Wei XH, Cheng XH et al. Yao xue xue bao = Acta pharmaceutica Sinica 2016; 51:75-79. The study was designed to explore the drug-drug interactions mechanisms mediated by OATP1B1 between traditional Chinese medicine Danshensu and
rosuvastatin. First, the changes of rosuvastatin pharmacokinetics were investigated in presence of Danshensu in rats. Then, the primary rat hepatocytes model was established to explore the effects of Danshensu on the uptake of rosuvastatin by hepatocytes. Finally, HEK293T cells with overexpression of OATP1B1*a and OATP1B1*5 were established using a lentiviral delivery system to explore the effects of Danshensu on the uptake of rosuvastatin. Rosuvastatin pharmacokinetic parameters of C(max0, AUC(0-t), AUC(0-infinity) were increased about 123%, 194% and 195%, by Danshensu in rats, while the CL z/F value was decreased by 60%. Uptake of rosuvastatin in the primary rat hepatocytes was decreased by 3.13%, 41.15% and 74.62%, respectively in the presence of 20, 40 and 80 mumol x L(-1) Danshensu. The IC50 parameters was (53.04 +/- 2.43) mumol x L(-1). The inhibitory effect of Danshensu on OATP1B1 mediated transport of rosuvastatin was related to the OATP1B1 gene type. In OATP1B1*5-HEK293T mutant cells, transport of rosuvastatin were reduced by (39.11 +/- 4.94)% and (63.61 +/- 3.94)% respectively, by Danshensu at 1 and 10 mumol x L(-1). While transport of rosuvastatin was reduced by (8.22 +/- 2.40)% and (11.56 +/- 3.04)% and in OATP1B1*1a cells, respectively. Danshensu significantly altered the pharmacokinetics of rosuvastatin in rats, which was related to competitive inhibition of transport by OATPBJ1. Danshensu exhibited a significant activity in the inhibition of rosuvastatin transport by OATP1B1*5-HEK293T, but not by OATP1B1*1a, suggesting a dependence on OATP1B1 sequence. PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27405165

[68] Development of Advanced Atherosclerotic Plaque by Injection of Inflammatory Proteins in a Rabbit Iliac Artery Model. Kim JS, Lee SG, Oh J et al. Yonsei medical journal 2016; 57:1095-1105.PURPOSE: Appropriate animal models of atherosclerotic plaque are crucial to investigating the pathophysiology of atherosclerosis, as well as for the evaluation of the efficacy and safety of vascular devices. We aimed to develop a novel animal model that would be suitable for the study of advanced atherosclerotic lesions in vivo. MATERIALS AND METHODS: Atherosclerotic plaque was induced in 24 iliac arteries from 12 rabbits by combining a high cholesterol diet, endothelial denudation, and injection into the vessel wall with either saline (n=5), olive oil (n=6), or inflammatory proteins [n=13, high-mobility group protein B1 (HMGB1) n=8 and tumor necrosis factor (TNF)-alpha n=5] using a Cricket Micro-infusion catheter. Optical coherence tomography (OCT) was performed to detect plaque characteristics after 4 weeks, and all tissues were harvested for histological evaluation. RESULTS: Advanced plaque was more frequently observed in the group injected with inflammatory proteins. Macrophage infiltration was present to a higher degree in the HMGB1 and TNF-alpha groups, compared to the oil or saline group (82.1+/−5.1% and 94.6+/−2.2% compared to 49.6+/−14.0% and 46.5+/−9.6%, p-value<0.001), using RAM11 antibody staining. On OCT, lipid rich plaques were more frequently detected in the inflammatory protein group [saline group: 2/5 (40%), oil group: 3/5 (50%), HMGB1 group: 6/8 (75%), and TNF-alpha group: 5/5 (100%)]. CONCLUSION: These data indicate that this rabbit model of atherosclerotic lesion formation via direct injection of pro-inflammatory proteins into the vessel wall is useful for in vivo studies investigating atherosclerosis. PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27401639
Early Effects of Intensive Lipid-Lowering Treatment on Plaque Characteristics Assessed by Virtual Histology Intravascular Ultrasound. Lee JH, Shin DH, Kim BK et al. Yonsei medical journal 2016; 57:1087-1094. PURPOSE: The effects of short-term intensive lipid-lowering treatment on coronary plaque composition have not yet been sufficiently evaluated. We investigated the influence of short-term intensive lipid-lowering treatment on quantitative and qualitative changes in plaque components of non-culprit lesions in patients with acute coronary syndrome. MATERIALS AND METHODS: This was a prospective, randomized, open-label, single-center trial. Seventy patients who underwent both baseline and three-month follow-up virtual histology intravascular ultrasound were randomly assigned to either an intensive lipid-lowering treatment group (ezetimibe/simvastatin 10/40 mg, n=34) or a control statin treatment group (pravastatin 20 mg, n=36). Using virtual histology intravascular ultrasound, plaque was characterized as fibrous, fibro-fatty, dense calcium, or necrotic core. Changes in plaque components during the three-month lipid-lowering treatment were compared between the two groups. RESULTS: Compared with the control statin treatment group, there was a significant reduction in low-density lipoprotein cholesterol in the intensive lipid-lowering treatment group (-20.4+/-17.1 mg/dL vs. -36.8+/-17.4 mg/dL, respectively; p<0.001). There were no statistically significant differences in baseline, three-month follow-up, or serial changes of gray-scale intravascular ultrasound parameters between the two groups. The absolute volume of fibro-fatty plaque was significantly reduced in the intensive lipid-lowering treatment group compared with the control group (-1.5+/-3.4 mm(3) vs. 0.8+/-4.7 mm(3), respectively; p=0.024). A linear correlation was found between changes in low-density lipoprotein cholesterol levels and changes in the absolute volumes of fibro-fatty plaque (p<0.001, R(2)=0.209). CONCLUSION: Modification of coronary plaque may be attainable after only three months of intensive lipid-lowering treatment. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27401638