Apolipoprotein A-IV in health and disease

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There exists accumulating evidence from in vitro studies that apolipoprotein A-IV (apoA-IV) plays an important role in reverse cholesterol transport. Our group focuses on the following research issues related to apoA-IV:

ApoA-IV in patients with atherosclerotic complications: We demonstrated for the first time that decreased plasma concentrations of apoA-IV are associated with atherosclerotic complications. This association was observed in the general population as well as in patients with kidney disease **[1,2]**.

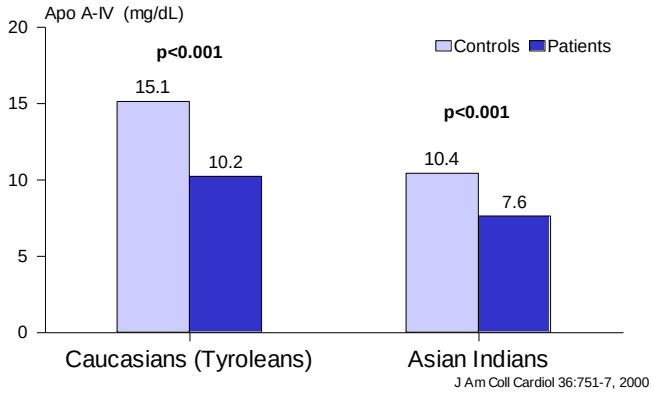

Figure 1: *ApoA-IV plasma concentrations in patients with coronary artery disease and healthy controls. Data are provided for a Caucasian as well as an Asian Indian group of patients and controls.*

ApoA-IV in patients with renal disease: In patients with renal disease we observed that apoA-IV concentrations start to increase during the earliest phases of renal impairment which makes apoA-IV to an early marker of renal impairment **[3]**. Dialysis patients have twice as high plasma concentrations than healthy controls **[4,5]**. In the "Mild to Moderate Kidney Disease Study" (MMKD) we found that the presence of high concentrations of apoA-IV is a reliable predictor for a progression of kidney disease during the following years of observation. This association was independent from the baseline glomerular filtration rate and proteinuria **[2]**.

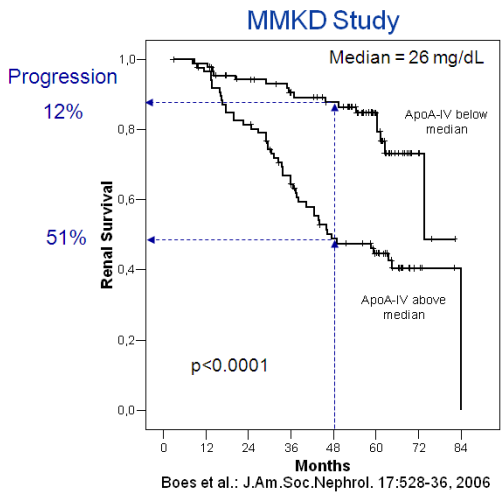

Figure 2: *Results from the "Mild to Moderate Kidney Disease" (MMKD) Study on progression of kidney disease. Kaplan-Meier curves of renal endpoints in patients with infra- and supramedian plasma apoA-IV concentrations.*

Ongoing work

- We are investigating the usability of apoA-IV as predictor of atherosclerosis, kidney impairment and components of the metabolic syndrome in large scale epidemiological projects. This work is done in cross-sectional and prospective cohort studies as well as in case-control studies of various diseases.
- We aim to identify genes which genetically determine apoA-IV plasma concentrations using genome-wide association studies.

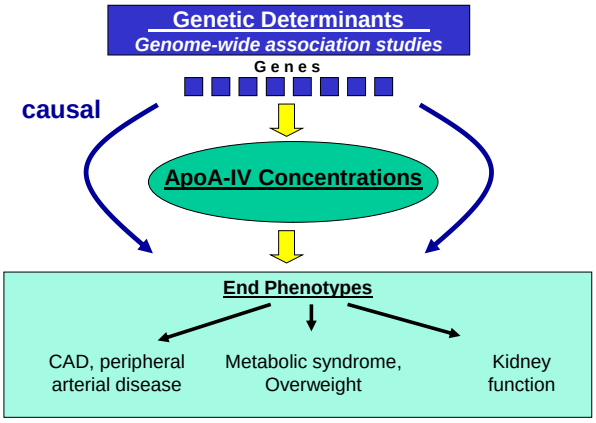

Figure 3: *Schematic illustration of the ongoing projects.*

Team members:

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Main collaborators:

KORA Study Group, SAPHIR Study, Utah Obesity Case-Control Study, CAVASIC Study

Selected Publications:

1. Kronenberg F, Stühlinger M, Trenkwalder E, Geethanjali FS, Pachinger O, Von Eckardstein A, Dieplinger H: Low apolipoprotein A-IV plasma concentrations in men with coronary artery disease. ***Journal of the American College of Cardiology*** 36: 751-757, 2000. [PubMed]
2. Boes E, Fliser D, Ritz E, König P, Lhotta K, Mann JFE, Müller GA, Neyer U, Riegel W, Riegler P, Kronenberg F, for the MMKD Study Group: Apolipoprotein A-IV predicts progression of chronic kidney disease: The Mild to Moderate Kidney Disease (MMKD) Study. ***Journal of the American Society of Nephrology*** 17:528-536, 2006. [Pub-Med]
3. Kronenberg F, Kuen E, Ritz E, Junker R, König P, Kraatz G, Lhotta K, Mann JFE, Müller GA, Neyer U, Riegel W, Riegler P, Schwenger V, Von Eckardstein A: Apolipoprotein A-IV serum concentrations are elevated in mild and moderate renal failure. ***Journal of the American Society of Nephrology*** 13: 461-469, 2002. [PubMed]
4. Kronenberg F, König P, Neyer U, Auinger M, Pribasnig A, Lang U, Reitinger J, Pinter G, Utermann G, Dieplinger H: Multicenter study of lipoprotein(a) and apolipoprotein(a) phenotypes in patients with end-stage renal disease treated by hemodialysis or continuous ambulatory peritoneal dialysis. ***Journal of the American Society of Nephrology*** 6: 110-120, 1995. [PubMed]
5. Kronenberg F, Lingenhel A, Neyer U, Lhotta K, König P, Auinger M, Wiesholzer M, Andersson H, Dieplinger H: Prevalence of dyslipidemic risk factors in hemodialysis and CAPD patients. ***Kidney International*** 63, Suppl. 84: S113-S114, 2003. [PubMed]
6. Ezeh B, Haiman M, Alber HF, Kunz B, Paulweber B, Kraft HG, Weidinger F, Pachinger O, Dieplinger H, Kronenberg F: Plasma distribution of apoA-IV in patients with coronary artery disease and healthy controls. ***Journal of Lipid Research*** 44: 1523-1529, 2003. [PubMed]