Study Group Genetic Epidemiology of Kidney Disease

Study Group Members

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Dr Böger graduated from medical school at the Ludwig-Maximilians-Universität Munich in Germany. He completed his residency for Internal Medicine at the Ludwig-Maximilians-University Hospital Munich and the University Medical Center of Regensburg. In Regensburg he completed a fellowship in Nephrology and is Attending for the Nephrology Department since April 2008.

His research interests lie in genetic epidemiology of renal traits in the general population and of diabetes-associated end points.

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Genetic epidemiology of complex renal traits

Heritability studies have shown that 30-40% of the variability of renal function (glomerular filtration rate, GFR) and urinary albumin excretion (albuminuria) are explained by genetic factors. This has been shown in general population studies and in disease specific cohorts, such as patients with diabetes mellitus.

With the method of genome wide association analysis (GWAS), genetic variants of the whole genome are systematically analysed for association with specific phenotypes such as eGFR, or albuminuria, or kidney disease.

In collaboration with Iris M. Heid (Dept. of Genetic Epidemiology, University of Regensburg), we are active participants in the Analyst Group of the CKDGen Consortium. CKDGen is an international collaboration of population based studies dedicated to unravelling the genetics renal traits such as eGFR and albuminuria, using GWAS meta-analysis.

Epidemiology of diabetes-associated micro- and macrovascular end points

Almost 10% of the general population have type 2 diabetes, and diabetes is associated with a significant increase in micro- and macrovascular morbidity. After 10 years of diabetes, about 25% develop diabetic nephropathy, which can progress to end stage renal disease. Hypertension and blood glucose control explain only part of the risk for diabetes-associated complications. It is our aim to discover biomarker and genetic variants contributing to this risk.

To reach this goal, we have recruited two prospective cohorts with biomaterial banks of patients with diabetes mellitus type 2: DIACORE and GENDIAN (see “Current Projects”).
**Current projects**

**Genome wide association studies (GWAS) of eGFR, albuminuria and kidney function change over time**

As active members of the CKDGen Analyst Group, we are participating in GWAS meta-analyses of renal phenotypes in the CKDGen consortium since 2009 (see publications). Currently, more than 30 cohorts with a total of over 130000 individuals are participating in CKDGen’s endeavour to unravel the genetics of kidney traits.

Our group is contributing to this effort with the data sets of three cohorts:
- KORA F3 and KORA F4, representative samples of the general population recruited from the region around Augsburg, Germany.
- GENDIAN, a case control study of type-2-diabetes associated kidney disease.

Current CKDGen projects include GWAS of eGFR using 1000 Genomes imputed data sets and Exome Chip data sets. Further, completed meta-analyses of eGFR and albuminuria are currently in the stage of manuscript writing.

**Epidemiology of diabetes mellitus type 2 associated end points in**

We have recruited two cohorts for the study of micro- and macrovascular end points in patients with diabetes mellitus type 2:

1. **DIACORE (DIAbetes COhoRtE, [http://www.diacore.de](http://www.diacore.de), PI: Carsten A. Böger)** is a prospective cohort study of 3000 patients of self-reported Caucasian ethnicity with prevalent diabetes mellitus type 2 (DM2), recruited between 2/2010 and 3/2014. 2-year follow-up examinations are planned every 2 years for 10 years. The first follow-up examination has started in August 2013. Study visits are performed in University-based recruiting clinics in Germany using standard operating procedures. All prevalent DM2 patients in outpatient clinics surrounding the recruiting centers are invited to participate. At baseline and at each 2-year follow-up examination, patients are subjected to a core phenotyping protocol. This includes a standardized online questionnaire and physical examination to determine incident micro- and macrovascular DM2 complications, malignancy and hospitalization. Confirmatory outcome information is requested from patient records. Blood samples are obtained for a centrally analyzed standard laboratory panel and for biobanking of aliquots of serum, plasma, urine, mRNA and DNA for future scientific use. A subset of the cohort is subjected to extended phenotyping, including sleep apnea screening, skin autofluorescence measurement, non-mydriatic retinal photography and non-invasive determination of arterial stiffness.

Reference:
2. **GENDIAN (GENetics of DIAbetic Nephropathy, PI: Carsten A. Böger)** is a case control study of diabetes associated nephropathy in Caucasian subjects. Cases are n=438 prevalent patients on maintenance hemodialysis due to diabetic nephropathy, recruited from 30 dialysis centers in Southern Germany between August 1999 and January 2000, and n=84 patients with biopsy proven diabetic nephropathy. A total of n=450 controls not on renal replacement therapy were recruited in a large diabetes clinic in Southern Germany (Diabetes Zentrum Mergentheim). Follow-up examinations were performed in all cases and controls to assess incident cardiovascular events.

References:
Collaborations

Prof. Dr. Iris Heid
Department of Genetic Epidemiology, Institute of Epidemiology and Preventive Medicine

CKDGen consortium

Institute for Genetic Epidemiology, Helmholtz-Zentrum München
(Director: Prof. Dr. Konstantin Strauch).
http://www.helmholtz-muenchen.de

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University Medical Center of Regensburg
Publications
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13. Götz AK*, Böger CA*, Hirschmann C, Schmitz G, Riegger GAJ, Krämer BK. Effect of HMG-CoA-reductase inhibitors on survival in type 2 diabetes patients with end stage...


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