Wake Forest® School of Medicine

Information for Clinicians and Investigators

Studies of Autosomal Dominant Interstitial Kidney Diseases : *UMOD, REN and MUC1*

Background

Autosomal Dominant Interstitial Kidney Diseases (ADIKD) include conditions previously known as medullary cystic kidney disease. These conditions are characterized by:

1. Autosomal dominant inheritance, in a similar manner to polycystic kidney disease.
2. Bland urinary sediment with minimal protein.
3. Renal ultrasounds usually showing normal or small kidneys.

The most common causes of these conditions include *UMOD*, *REN* and *MUC1* conditions, though there are other causes for which the gene has not been found.

Dr. Bleyer and his colleagues at Wake Forest collaborate with Dr. Stanislav Kmoch at the Charles University First Faculty of Medicine in Prague, Czech Republic, scientists at the Broad Institute Cambridge, MA and the National Institutes of Health Bethesda, MD to further investigate these diseases.

We believe that collaboration provides the best opportunity to make diagnoses and to find treatments for the conditions that we study.

Progress

Over the last 14 years, we have evaluated 400 different families for inherited kidney disease. From these families, we have identified patients with:

1. *UMOD* mutations encoding Uromodulin or Tamm Horsfall Protein that cause MCKD2.
2. *REN* mutations encoding RENIN as another cause of ADIKD.
3. *MUC1* mutations encoding MUC1 that cause MCKD1.

We have created patient education information and websites in order to increase awareness of these conditions and to educate affected families.

Further working with these families, we have also studied the clinical characteristics of these conditions and published our findings (see Publications).

Future goals

1. We are interested in helping other investigators determine if there is *UMOD, REN* or *MUC1* disease in families under their care.
2. We are interested in identifying more genetic causes of inherited kidney disease. Dr. Kmoch in Prague is able to perform whole exome analysis, and we are in the process of trying to identify genetic causes of similar conditions.
3. We are creating registries of affected individuals with these mutations. We are trying to obtain as many past values of serum creatinine for each individual as possible in order to study disease progression and identify risk factors for these conditions.
4. We are involved in basic science research in these conditions to attempt to find a cure for these diseases.

Our overall goal is to help identify causes of inherited kidney disease, but more importantly, to find effective treatments for these conditions.

Opportunities for collaboration

We believe that coordinated study of these conditions will be the most effective means to find new methods of treatment. Following are some of the means by which we are working with others to make this happen:

1. **Evaluation of families with inherited kidney disease.** If you have a family that you believe may have *MUC1, UMOD, REN* mutations, or another cause of inherited kidney disease of uncertain cause, contact Dr. Bleyer at ableyer@wakehealth.edu We have significant experience in the evaluation and diagnosis of these disorders. We can facilitate testing for these disorders, often in a research setting at no cost to the patient.
2. **Affected individuals with known *MUC1, UMOD* or *REN* mutations.** We have patient education materials available for these disorders. We are also interested in enrolling these individuals in our clinical trials to help study factors affecting progression. This involves obtaining medical records and entering laboratory values in a registry that we have created. The more families that we have with these disorders, the more we are able to understand factors affecting progression.
3. **Study of individual *UMOD* mutations**. We have created a map of *UMOD* mutations that helps to predict age of onset of ESRD for individual families and provides information as to whether mutations are likely to cause disease or be clinically silent. We are trying to collect information on as many mutations as possible. If you have a family with a *UMOD* mutation, we would be most interested to learn about the site of the mutation so that we could enter it in our UMOD mutation map. This in turn will help other clinicians finding similar mutations.
4. **Use of our registry for analysis.** We are willing to provide data from our registry to others to be used for analysis.
5. **Biologic samples.** We have limited biologic materials from patients with these disorders. We are especially interested in obtaining as many biopsy samples as possible on individuals with known *MUC1* mutations.

   For any patients who may be undergoing nephrectomy, we have found that obtaining fresh kidney tissue is very helpful in our research. We would especially like to establish cell lines from a kidney of a patient with a UMOD mutation.
6. **We are establishing cell lines and antibodies for *MUC1* disease.** We are developing methodologies to supply these cell lines to investigators at their request.

For more information

Please contact Dr. Bleyer at ableyer@wakehealth.edu or 336-716-4513. We are happy to provide further information and answer any questions you may have.

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Or visit us on the web at:
www.wakehealth.edu/Nephrology/Inherited-Kidney-Disease
www.wakehealth.edu/Nephrology/Medullary-Kidney-Disease
www.wakehealth.edu/Nephrology/Gout-Kidney-Disease

We believe that collaboration provides the best opportunity to find treatments for the conditions that we study.

Publications

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17. Bleyer AJ, Woodard AS, Shihabi Z, et al. Clinical characterization of a family with a mutation in the uromodulin (Tamm-Horsfall glycoprotein) gene. *Kidney Int* 64(1):36-42, 2003
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