



Joseph Lagas, Doctoral Candidate in Molecular Biology (Washington University in St. Louis), generously agreed to provide layman's summaries of two Alport-centric research papers published in late March 2021.

Genotype–phenotype correlations and nephroprotective effects of RAAS inhibition in patients with autosomal recessive Alport syndrome

Zhang, Yanqin et al.

Pediatric Nephrology, March 27, 2021.

Alport syndrome is caused by mutations in specific genes which produce products that form key structures within the kidney. Most patients have mutations in a gene on the X chromosome (X linked Alport syndrome) however, there are still many patients with mutations in other genes that are not X-linked. These patients have been neglected so far and this study attempts to understand how one of these groups (autosomal recessive Alport syndrome patients) progress towards kidney failure and if ACE and ARB inhibitors are effective at delaying kidney failure. The researchers found that this treatment was beneficial for these patients in extending their kidney function. Additionally, they found that certain mutations called non-missense mutations (large alterations to the gene product) caused kidney decline much faster than missense mutations (slight alterations to the gene product). Patients with autosomal recessive Alport syndrome can rest easy knowing that using ACE/ARB inhibitors is beneficial for them and it is becoming more important that we all understand that performing genetic testing is helpful for predicting the severity of this disease.

Metformin ameliorates the severity of experimental Alport syndrome

Omachi, Kohie et al.

Scientific Reports, March 29, 2021.

Alport syndrome patients are normally treated with some combination of ACE and ARB inhibitors to prolong their kidney function as long as possible. However, some patients cannot tolerate these drugs or face additional problems such as increasing side effects which stops them from taking this medication. This study wanted to determine if metformin, a drug used in treatment of type 2 diabetics, may be beneficial in Alport patients as an alternative to the normal treatments. They tested metformin in mice with Alport syndrome and compared it to losartan treated mice (a common ARB used in Alport treatment). They found that metformin was beneficial in treating several symptoms of Alport syndrome such as proteinuria, serum creatinine, and kidney dysfunction. In some measures, losartan was still better for the kidneys of these mice but generally, metformin proved to be a potentially suitable alternative. The combination of losartan and metformin was more effective at treating Alport syndrome than using losartan or metformin alone. These results show that metformin could be used to treat Alport syndrome patients and could serve as a potential alternative to the normal medications once a clinical trial proves it's effective.