MICRO-RNA REGULATED PODOCYTE - GLOMERULAR BASEMENT MEMBRANE INTERACTION IN PROTEINURIC KIDNEY DISEASE

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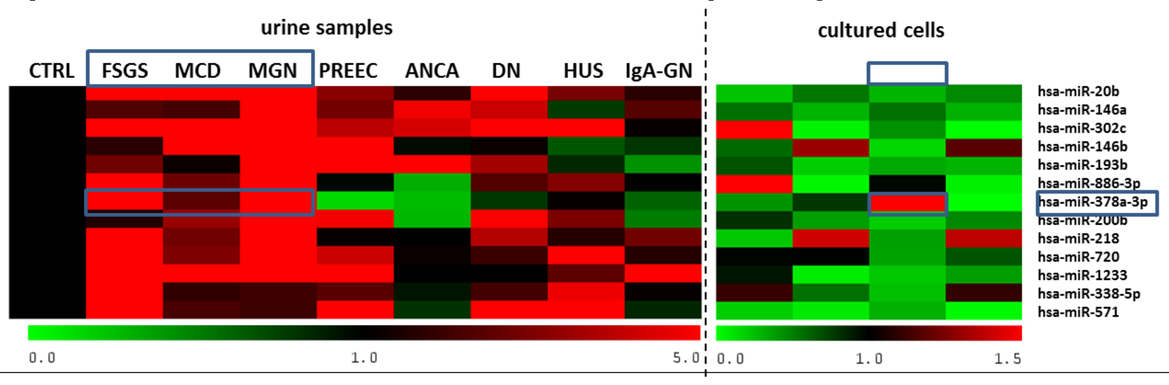
Background

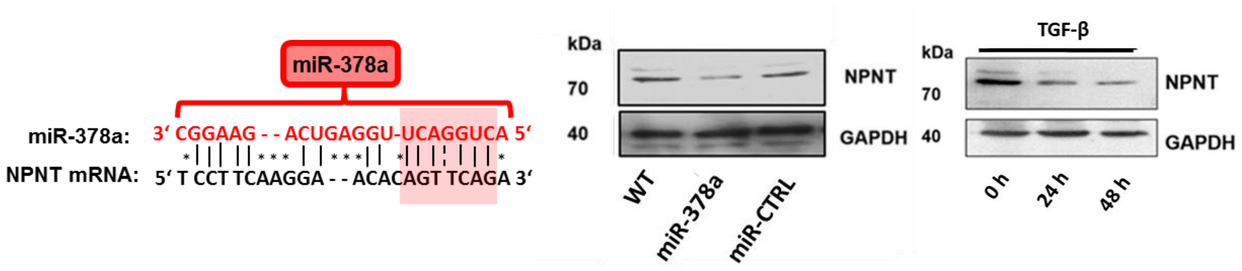
Despite the description of causative gene mutations, circulating factors and autoantibodies the pathophysiology of many proteinuric kidney diseases is still incompletely understood. MicroRNAs (miRs) play an important role in gene regulation and therefore seem to be promising candidates involved in glomerular diseases.

Results

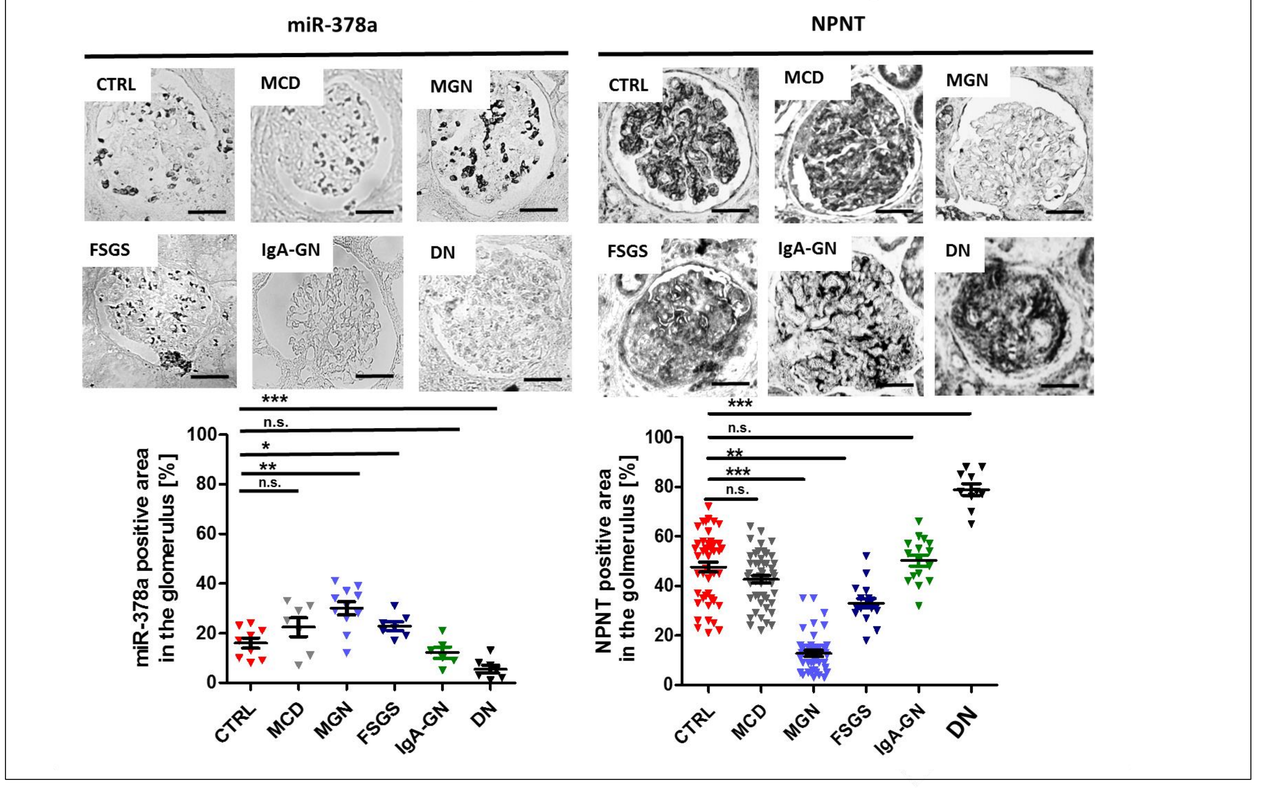
1. MiR-378a is upregulated in urines samples from patients with nephrotic diseases as well as in stressed podocytes.



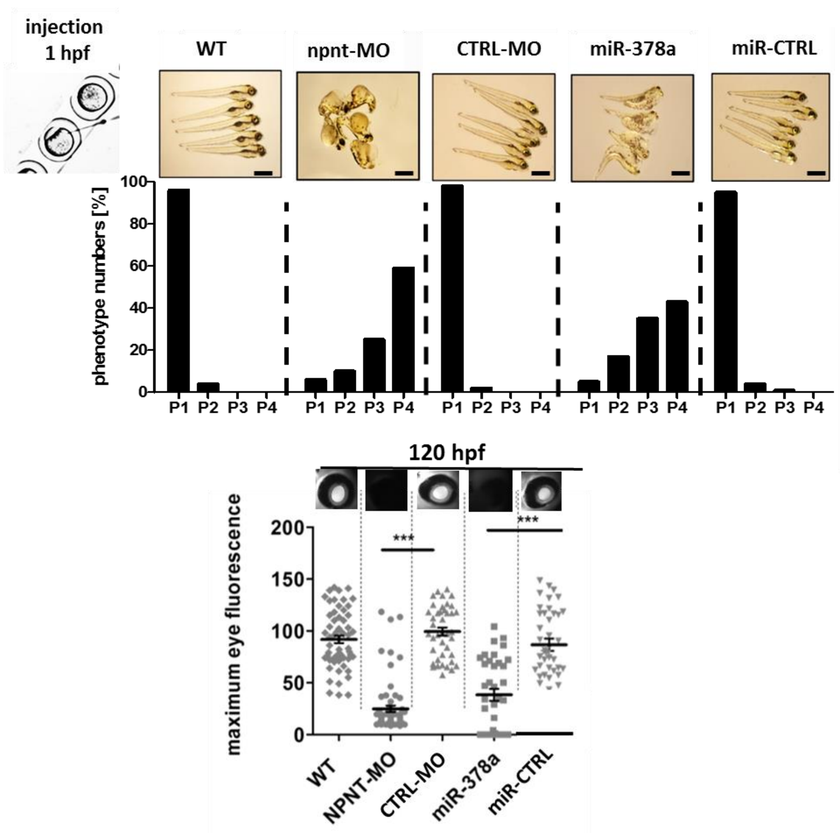
2. NPNT is a target of miR-378a and regulated by TGF-β

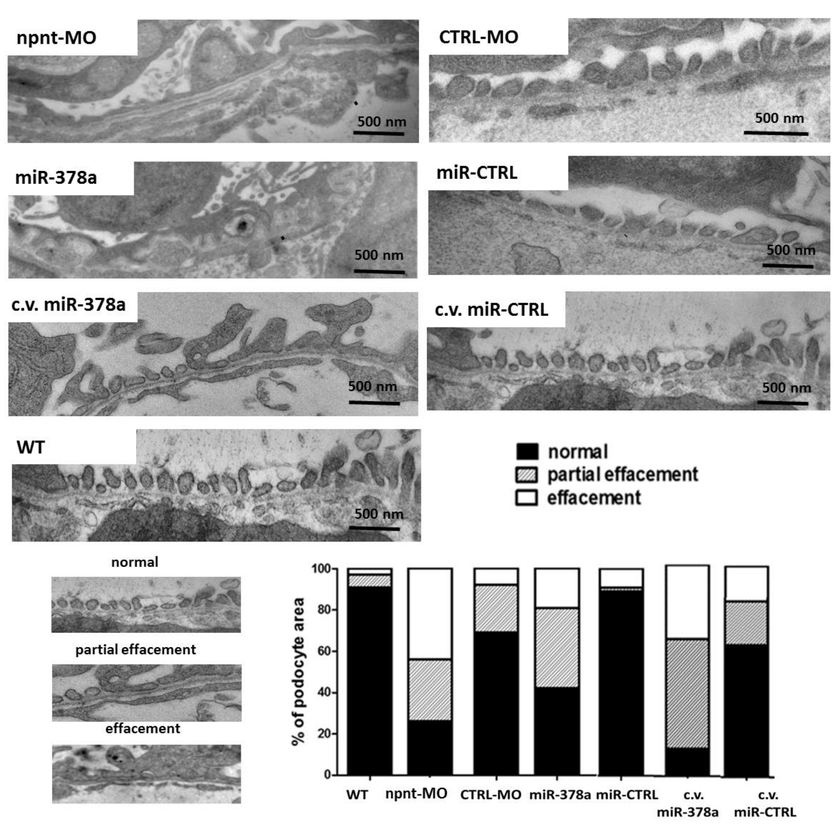


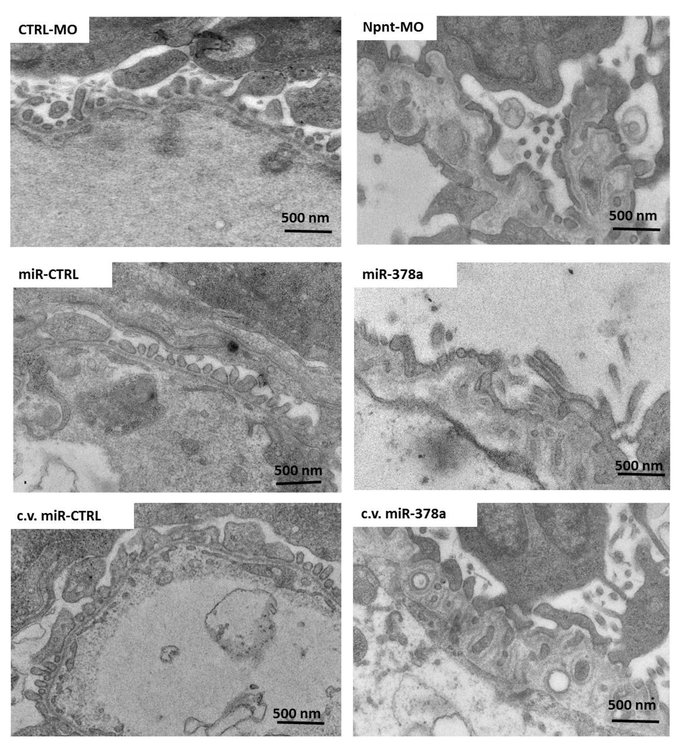
3. MiR-378a and NPNT expression are altered in glomerular diseases.



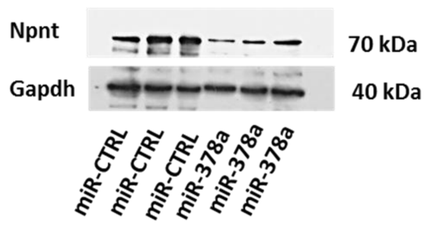
4. Morpholino induced npnt knockdown or miR-378a overexpression induces loss of plasma proteins, edema, podocyte foot process effacement and GBM changes in zebrafish larvae.

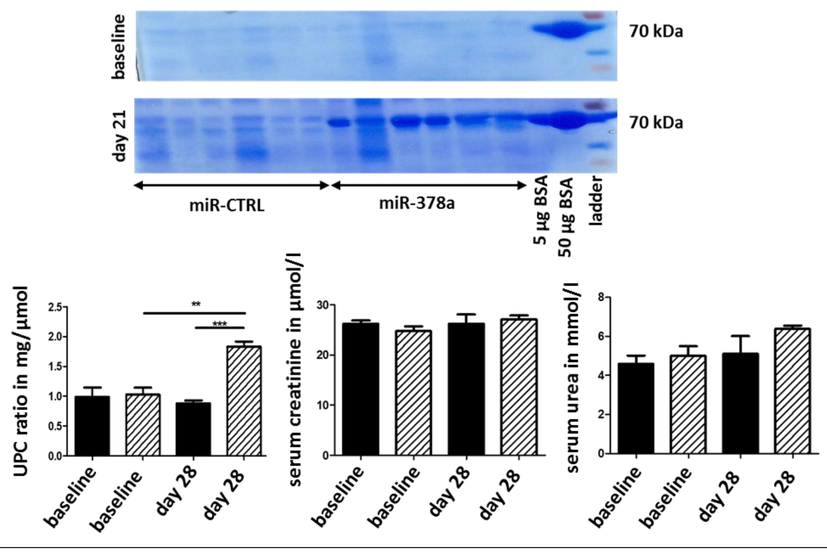


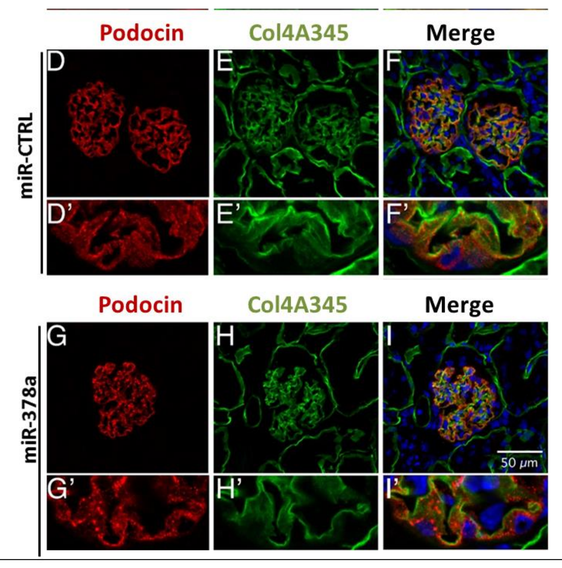


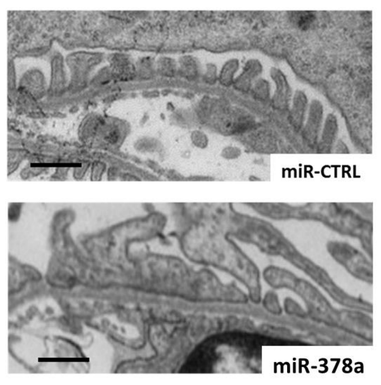


5. MiR-378a overexpression leads to albuminuria, podocyte effacement as well as altered expression of podocyte proteins in mice.









Conclusion

In summary, we demonstrate that miR-378a is an important regulator of proteinuria development, which exerts its function through regulation of nephronectin. Thus, miR-378a controlled nephronectin expression is a novel mechanism for proteinuria development in active glomerular diseases.

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