Human organoid system based therapy discovery & development for age-related macular degeneration (ReDiMoAMD)

Mike O. Karl

Project Coordinator:

Mike O. Karl, TU Dresden, CRTD - Center for Regenerative Therapies Dresden, Dresden, Germany

Project Partners:

Marius Ader, TU Dresden, CRTD, Dresden, Germany
Deniz Dalkara, Institut de la Vision, Paris, France
Julien Muffat, Hospital for Sick Children, Toronto, Canada
Nicola Zamboni, ETH Zürich, Inst. Of Molecular Systems Biology, Zürich, Switzerland

Age-related macular degeneration (AMD) causes vision loss due to outer retinal atrophy, but disease models for the neural retina and therapies are missing. Photoreceptor cell transplantation represents a promising treatment approach, but clinical translation remains a challenge. Our consortium aims to bridge two related research gaps: modeling of AMD pathology and therapy development (preventive and restorative). We developed a human retinal organoid model with cellular and molecular AMD hallmarks. The photoreceptor pathomechanisms in this model might offer targets to prevent AMD and to restore it by photoreceptor transplantation – since both might share common and/or interrelated processes. For example, metabolic stress and inflammation, which are key in AMD, and known triggers of neurodegeneration in other organs, might cause photoreceptor atrophy and affect transplant integration success. Thus, the aims of the consortium are to develop, optimize and apply organoid and viral tools to decipher pathomechanisms by comparing our human and mouse models, determining the functions of inflammation (microglia) and metabolic changes. We will explore latter findings in preclinical studies to find potential targets for therapeutic prevention of pathogenesis and optimization of photoreceptor transplantation.