

**PROJECT 2 (optional)**DoS: Prof. Francesco BandelloTitle: Conjunctival impression cytology miRNAs evaluation in diabetic macular edema.Curriculum: Experimental and Clinical MedicineResidency Program: OphthalmologyLink to OSR/UniSR personal page: <https://www.hsr.it/clinica/specialita-cliniche/oculistica/francesco-bandello/>**Project description** (Number of characters, including spaces: 2.000 - 3.000):

Diabetic retinopathy (DR) is one of the leading causes of blindness in the occidental world; it affects approximatively one third of diabetic patients, with an incremental trend. Key factors for the pathogenesis of DR is represented by microvascular dysfunctions and inflammation. These phenomena are also promoted by the increased oxidative stress following the hyperglycemia status. While vascular perfusion deficits and inflammation make worse, DR progresses to advanced stages and it can develop also two frequent complications, namely diabetic macular edema (DME) and neovascular proliferations. To date, DME is well treated by means of anti-VEGF or steroids intravitreal treatments. The response to intravitreal treatment is highly variable as well as the reachable visual outcome. This depends by several factors. In particular, it is known that DME is the final effect of the combined action of pro-inflammatory cytokines and VEGF release, and microvascular alterations leading to blood retinal barrier breakdown. However, these components may contribute in different ways to the onset and progression of DME; this is the reason why the response to intravitreal treatments is not univocal. Recent evidences demonstrated a role of noncoding RNAs, especially microRNAs (miRNAs), on the onset and progression of several diseases. In healthy context, miRNAs participate in cell metabolism, metabolic pathways and oxidative stress regulation. A meaningful role of miRNAs dysregulation was found both in type I and type II diabetes. With respect to the role of miRNAs in ophthalmologic field, it was already demonstrated how their evaluation, through the isolation from conjunctival impression cytology, represents a useful and feasible way to evaluate ocular inflammation. The main aim of the present project is to dose conjunctival miRNAs, by means of impression cytology, in patients affected by naïve DME and undergoing intravitreal treatments with anti-VEGF or steroids, to assess miRNAs role in the evaluation of patients' response to treatment. These patients will undergo anti-VEGF or steroids intravitreal treatments, in accordance with classic clinical settings; the final outcome evaluation will be evaluated after one year of treatment. In particular, both visual acuity and retinal structural changes, evaluated by means of structural optical coherence tomography (OCT) biomarkers, will be evaluated. In particular, the following parameters will be measured: central macular thickness, choroidal thickness, retinal thickness, subretinal fluid and hyperreflective foci.

This study might potentially provide a new biomarker, namely conjunctival miRNAs, to predict patients' response to intravitreal treatments. In particular, miRNAs evaluation might represent an extremely feasible way to detect different DME patients' subgroups, thus having an important role for the proper choice of the intravitreal drug. The project will be supported by adequate funding sources.

**Skills to be acquired by the student:**

This project will allow the student to acquire the following skills: research conduction, analysis & problem-solving, critical thinking, team working and collaboration, adaptability, curiosity, communication, managing data and information, innovation, writing reports.

**References (max. 3)**

- Lee R, Wong TY, Sabanayagam C. Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. *Eye Vis (Lond)*. 2015;2:17.
- Schmidt-Erfurth U, Garcia-Arumi J, Bandello F, Berg K, Chakravarthy U, Gerendas BS, Jonas J, Larsen M, Tadayoni R, Loewenstein A. Guidelines for the Management of Diabetic Macular Edema by the European Society of Retina Specialists (EURETINA). *Ophthalmologica*. 2017;237(4):185-222.
- Mastropasqua R, Toto L, Cipollone F, Santovito D, Carpineto P, Mastropasqua L. Role of microRNAs in the modulation of diabetic retinopathy. *Prog Retin Eye Res*. 2014;43:92-107.