Role of P2X7 receptor in early diabetic retinopathy

1)Bucolo C. 2)Platania CB. 3)Giurdanella G. 4)Di paola L. 5)Leggio GM. 6)Salomone S. 7)Drago F.

University of Catania

Diabetic retinopathy (DR) is the most frequent complication of diabetes and one of leading causes of blindness worldwide. Early phases of DR are characterized by retinal pericyte loss mainly related to concurrent inflammatory process (1). Recently, an important link between P2X7 receptor (P2X7R) and inflammation has been demonstrated indicating this receptor as potential pharmacological target in DR (2). Here we first carried out an in silico molecular modeling study in order to characterize the allosteric pocket in P2X7R and identify a suitable P2X7R antagonist through molecular docking. Homology modeling, protein contact network analysis, molecular docking, MM-GBSA calculations were carried out in order to built and validate an in silico approach aimed in finding new ligands, selective toward the P2X7 receptor. The most promising P2X7 inhibitor has been tested on human retinal pericytes, cultured with high glucose levels (25 mM). The effects of the P2X7 inhibitor have been assessed by cell viability, LDH and IL-1β levels. Our data suggested that P2X7 receptor can be an interesting pharmacological target for diabetic retinopathy. Furthermore, our in silico/in vitro screening platform is suitable for discovery of new and effective P2X7 receptor inhibitors to manage the early phase of diabetic retinopathy.

References:

1. Hammes, H.P. et al. Diabetes (2011)

2. Karmakar, M. et al. Nature communications (2016)