



Neuroscience Center of Excellence

Seminar

"Group VIA calcium-independent phospholipase A₂ - possible pharmaceutical target in retinal diseases involving retinal pigment epithelium maintenance, proliferation and cell death"

Miriam Kolko, M.D., Ph.D.

University of Copenhagen
The Panum Institute
Copenhagen, Denmark

Calcium-independent phospholipase A₂ (iPLA₂) is a member of a rapidly growing super family of enzymes catalyzing the hydrolysis of membrane phospholipids in the *sn*-2 position thereby releasing free fatty acids and lysophospholipids. During the last decade expanding knowledge on the functions of iPLA₂ has been discovered and it is now clear that iPLA₂ is a multi-functional protein involved in various biological processes. Importantly, iPLA₂ has been shown to play a crucial role in macrophage phagocytosis, cell proliferation and cell death. Recently, we characterized iPLA₂ in the human retina. Retinal homeostasis is maintained by continuously phagocytosis of rod outer segments by the retinal pigment epithelium (RPE). Dysfunction of RPE phagocytosis is seen in retinal diseases such as i.e. age-related macula degeneration (AMD). We have established a model of RPE phagocytosis and have found an essential role of iPLA₂ in the regulation of this process. Furthermore, we have shown a role of iPLA₂ in RPE proliferation. During physiological conditions RPE is a non-proliferative tissue. However, during pathological conditions such as AMD, proliferative vitreoretinopathy (PVR) and as complication to vitreoretinal surgery, RPE begins to proliferate. RPE proliferation leads to the generation of scar like tissue in the retina and is followed by impaired vision. Thus, understanding of the mechanisms initiating RPE proliferation is essential in the development of pharmaceutical targets to treat a number of retinal diseases. We suggest that iPLA₂ may be one of the important targets in preventing RPE proliferation. In addition to RPE phagocytosis and proliferation our latest studies have revealed a role of iPLA₂ in RPE cell death. Overall, we hypothesize that iPLA₂ is important in retinal homeostasis and may play a crucial role during retinal damage.

Our ongoing and future studies therefore aim to further explore the role of iPLA₂ in retinal functioning as well as in retinal diseases leading to blindness.

**Wednesday November 7, 2007
4:00pm, Lion's Building, 8th Floor Conference Room
2020 Gravier Street, New Orleans, LA 70112**