

Roženica, Saturday, May 17 2025, 14:45-16:00

Location: dvorana Grandis

Session: **Roženica / Cornea**

Chairs: Vladimir Pfeifer and Petra Schollmayer

OR-084

Neuropsin, TRPV4 and intracellular calcium mediate intrinsic photosensitivity in corneal epithelial cells

Luka Lapajne¹, Monika Lakk², Christopher N. Rudzitis², Shruti Vemaraju³, Richard Lang³, Marko Hawlina¹, David Križaj²

¹Očesna klinika, Univerzitetni klinični center (UKC) Ljubljana, Slovenia

²Department of Ophthalmology & Visual Sciences, University of Utah School of Medicine, Salt Lake City, United States

³Department of Ophthalmology, College of Medicine, University of Cincinnati, Cincinnati, United States

Purpose: To investigate intrinsic phototransduction in the corneal epithelium and its role in intracellular and inflammatory signaling.

Methods: Optical imaging in isolated corneal epithelial cells (CECs) and debrided epithelia was combined with molecular, biochemical, pharmacological assays and gene deletion studies to track UVB-induced calcium signaling and release of cytokines, chemokines and matrix remodeling enzymes. Results from wild type mouse CECs were compared to data obtained from Opn5^{-/-} and Trpv4^{-/-} cells.

Results: UVB stimuli and TRPV4 activity induced epithelial release of IL-1 β , IL-17, matrix metalloproteinases MMP-3/MMP-9, and thymic stromal lymphopoietin (TSLP). UVB stimuli evoked [Ca²⁺]_i elevations in dissociated mouse CECs that were partially reduced by inhibition of TRPV4 channels, Trpv4 knockdown and replacement of control saline with Ca²⁺-free saline. UVB-induced Ca²⁺ responses were significantly suppressed by OPN5 deletion and by inhibition of phospholipase C signaling, and responses were abrogated in cells with depleted intracellular Ca²⁺ stores.

Conclusions: Mammalian CECs are intrinsically and constitutively photosensitive. UVB photons are transduced by neuropsin, phospholipase C and CICR signaling, with mouse but not human CE transduction exhibiting a UVB-sensitive TRPV4 component. TRPV4 activity and UVB transduction are linked to cell-autonomous release of proinflammatory, matrix remodeling and nociceptive interleukins and MMPs. TRPV4-induced cytokine release may contribute to the pain induced by mechanical injury of the cornea and CEC photosensing may alert and protect the visual system from ultraviolet B (UVB) radiation -induced snow blindness, injury, vision loss and cancer.

Nevropsin, TRPV4 in znotrajcelični kalcij posredujejo intrinzično fotosenzitivnost v celicah roženičnega epitela

Luka Lapajne¹, Monika Lakk², Christopher N. Rudzitis², Shruti Vemaraju³, Richard Lang³, Marko Hawlina¹, David Križaj²

¹Očesna klinika, Univerzitetni klinični center (UKC) Ljubljana, Slovenia

²Department of Ophthalmology & Visual Sciences, University of Utah School of Medicine, Salt Lake City, United States

³Department of Ophthalmology, College of Medicine, University of Cincinnati, Cincinnati, United States

Namen: Opredeliti intrinzično fototransdukcijo v roženičnem epitelu in njeno vlogo pri znotrajcelični in vnetni signalizaciji.

Metode: Slikanje z znotrajceličnim kalcijem (Ca²⁺ imaging) v celicah roženičnega epitela in odluščenem celotnem epitelu smo kombinirali z molekularnimi, biokemičnimi in farmakološkimi testi ter študijami z odstranjenima kopijema genov. Zanimalo nas je kakšno vlogo imajo spremembe koncentracije znotrajceličnega kalcija, povzročene z UVB sevanjem, na sproščanje citokinov, kemokinov in proteinov z vplivom na remodelacijo celičnega matriksa. Primerjali smo razlike med celicami divjega tipa miši in celicami iz Opn5^{-/-} in Trpv4^{-/-} živali.

Rezultati: UVB sevanje in aktivacija TRPV4 sta povzročila izločanje IL-1 β , IL-17, matriksnih metaloproteinaz MMP-3 in MMP-9 in timusnega stromalnega limfopoetina (TSLP) iz celic roženičnega epitela. Zvišanje koncentracije znotrajceličnega kalcija (Ca²⁺), povzročene z UVB sevanjem, je bilo delno zavrt s farmakološko blokado TRPV4 kanalov, odstranitvijo kopij genov za TRPV4 kanal ali odstranitvijo kalcijevih ionov iz kontrolne fiziološke raztopine. Odzivi Ca²⁺, povzročeni z UVB, so bili pomembno znižani z delecijo OPN5 in inhibicijo signaliziranja s fosfolipazo C ter zavrti v celicah z izčrpanimi zalogami znotrajceličnih kalcijevih ionov.

Zaključek: Celice roženičnega epitela sesalcev so intrinzično fotoobčutljive. UVB sevanje zaznavajo preko nevropsina, fosfolipaze C ter pri miših tudi deloma preko TRPV4 komponente. Aktivacija TRPV4 in UVB transdukcija sta povezani s sproščanjem proinflammatoryh citokinov, nociceptivnih interleukinov in matriksnih metaloproteinaz. S TRPV4 povzročeno sproščanje citokinov lahko prispeva k bolečini povzročeni z mehanskimi poškodbami, intrinzična UVB občutljivost pa lahko pripomore k zaščitnem vedenju in posledični zaščiti očesa pred škodljivim UVB sevanjem.

