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78. EXPLORING THE $\alpha 7$ NICOTINIC RECEPTOR IN HUMAN RETINAL PIGMENT EPITHELIUM CELLS AS A NOVEL THERAPEUTIC TARGET

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The $\alpha 7$ nicotinic acetylcholine receptor is highly expressed in the brain and is also present in non-neuronal cells, including immune and epithelial cells. It is involved in cognition, memory, pain, neuroprotection and inflammation and its potentiation has emerged as a therapeutic strategy for neurological, neurodegenerative, and inflammatory disorders. Given that the increase in oxidative stress in retinal pigment epithelial cells contributes to the development of age-related macular degeneration and that $\alpha 7$ activation exerts cell protective effects, we explored the presence and functional relevance of $\alpha 7$ in D407 retinal pigment epithelium cells, a model system for various retinal diseases. By real time PCR, and indirect immunofluorescence using confocal microscopy and flow cytometry we demonstrated the presence of $\alpha 7$ in these epithelial cells. To determine the presence of functional receptors, we measured the movement of intracellular calcium levels triggered by the activation of $\alpha 7$. A pulse of ACh together with an $\alpha 7$ positive allosteric modulator revealed a 3-fold increase in intracellular calcium measured with the fluo-3AM probe. To mimic the events occurring in age-related macular degeneration, we treated cells with ferric ammonium citrate (FAC) to induce stress damage and measured reactive oxygen species (ROS) with the fluorescent probe DCFH-DA. FAC treatment resulted in a significant increase in ROS levels with respect to the control. To determine if $\alpha 7$ protects against oxidative damage, we exposed cells to a specific $\alpha 7$ agonist, PNU-282987, before the FAC treatment. Notably, PNU-282987 exhibited protective effects against the damage, leading to a reduction in ROS levels compared to the treated cells. Overall, by identifying for the first time the presence of $\alpha 7$ in the D407 cell line and revealing its protective role against oxidative damage, we propose $\alpha 7$ as a promising therapeutic target for retinal neurodegenerative disorders.