Poly-ADP-ribose-polymerase activity contributes to photoreceptor cell death in the rd1 mouse

François Paquet-Durand, José Silva, Tanuja Talukdar, Leif Johnson, Stefanie Hauck, Marius Ueffing, Theo van Veen and Per Ekström

Department of Ophthalmology, Lund University, Sweden

GSF, Institute for Human Genetics, Neuherberg, Germany

Retinitis Pigmentosa (RP) is an inherited blinding disease for which there is currently no treatment available. It is characterized by a progressive loss of photoreceptors but the underlying mechanisms are poorly understood. Excessive activation of the enzyme poly-ADP-ribose-polymerase (PARP) has been shown to be involved in several neurodegenerative processes. To investigate a possible role of PARP in retinal photoreceptor degeneration, we used the rd1 mouse model for RP to study PARP expression and activity as well as the effects of PARP inhibition on photoreceptor viability. PARP expression was found to be equal when rd1 retina was compared with wild-type counterparts. In stark contrast to this, in situ analysis showed a dramatic and highly significant increase in PARP activity and PARylated proteins in rd1 photoreceptors undergoing cell death. Furthermore, PARP activity co-labelled with oxidatively damaged DNA and nuclear translocation of apoptosis inducing factor. The PARP specific inhibitor PJ34 reduced the number of dying cells in a short-term retinal culture paradigm and this protective effect translated into an increased number of surviving photoreceptors when the inhibitor was used in long-term retinal cultures. Taken together, our results demonstrate an involvement of PARP activity in rd1 photoreceptor degeneration. PARP inhibition may therefore be considered for the treatment of RP.