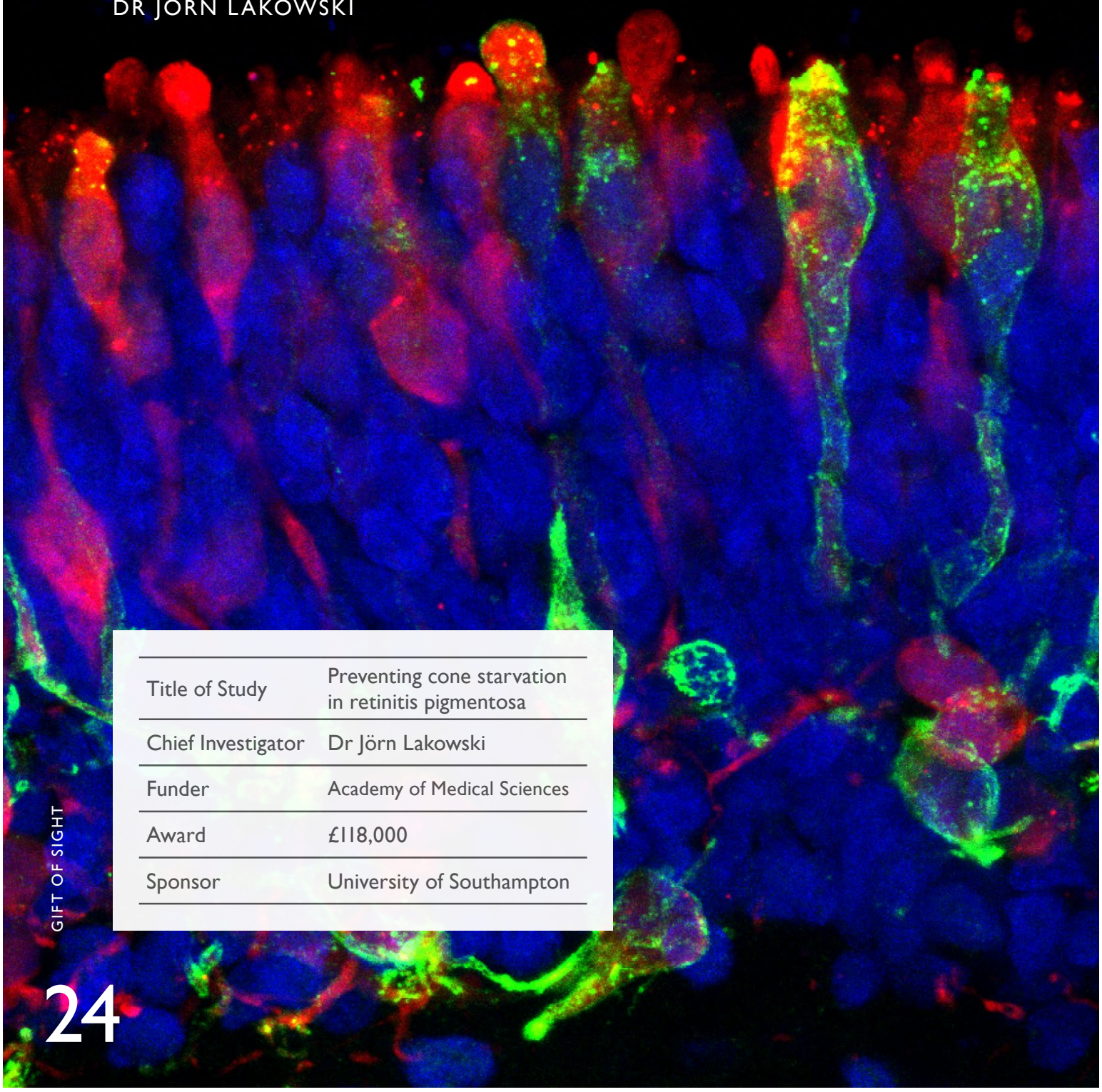
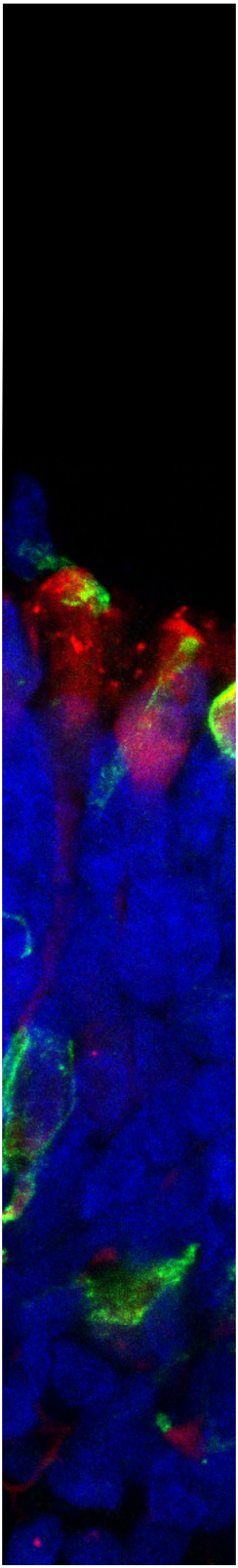
Current Research Studies

Preventing cone starvation in retinitis pigmentosa

DR JÖRN LAKOWSKI



Title of Study	Preventing cone starvation in retinitis pigmentosa
Chief Investigator	Dr Jörn Lakowski
Funder	Academy of Medical Sciences
Award	£118,000
Sponsor	University of Southampton



AN UNMET CLINICAL NEED.

Retinitis pigmentosa (RP) is a major cause of blindness worldwide with a prevalence of 1:4000. With over 80 disease-causing genes identified, RP is the most common type of inherited retinal degeneration. It is characterized by an initial loss of night vision as a result of the malfunction and death of rod photoreceptors. This early phase is followed by a loss of cone photoreceptors. Because cones are required for high-acuity and colour vision, their loss leads to a severe reduction in the quality of life as patients experience reduced autonomy, social isolation and challenges with activities of daily living.

Research has shown that cones depend on rods for a chemical survival signal, termed the "rod derived cone viability factor", which allows the cones to take up the necessary nutrients from their environment. As rods are lost during the course of the disease so is this signal, resulting in "starvation" and eventual loss of cones over time.

Unfortunately, this process is irreversible and there are no effective treatments available.

WHAT IS THIS PROJECT TRYING TO ACHIEVE?

Supported with a grant from the Academy of Medical Sciences this project aims to reveal the molecular machinery that triggers the death of cone photoreceptors in retinitis pigmentosa. Equipped with this knowledge we would then be able to devise methods to artificially replace the cone survival signal in the form of drugs.

HOW IS THIS RESEARCH CONDUCTED?

Obtaining rods and cones from patients suffering from RP is not possible. Instead, we have developed methods to grow "retinal organoids" or mini-retinas, using human stem cells in our laboratory. Employing the latest genome engineering technology, we have modified these mini-retinas in a way that now mimics the starvation of cones as experienced in RP. In addition, we have engineered the cones to emit a red fluorescent signal that allows us to visualize, track and isolate them for a range of applications. Using this system, we will grow in the lab large numbers of cones, expose them to stringent starvation conditions as seen in RP, and at the same time treat the cells with a chemical library, containing approximately 2000 clinically approved drugs. Those drugs found to mimic the cone survival signal and prevent cone death will be would form the basis of a future drug therapy for retinitis pigmentosa. The use of such repurposed drugs would significantly shorten the time that is required for clinical trials and translation into the clinical setting, as they are considered safe.

The stem cell team

Image on page 24 – Retina in a dish: cones grown within a retinal organoid from embryonic stem cells. Red: fluorescent cone specific reporter, green OPN1LW antibody staining.