On 16th July 2019, Prof. Geoff Higgins from the Oxford Institute of Radiation Oncology gave a lecture at the GRK Seminar with the title “Pre-clinical and clinical development of novel radiation sensitizers”. Prof. Higgins focuses on development of treatments that can be combined with radiotherapy to improve outcomes for cancer patients. His clinical work is strongly focused on lung cancer, as radiotherapy plays a key role in the treatment of this disease and is yet still associated with poor outcomes. In his talk he pointed out two strategies for obtaining of new radiation sensitizers:

1. Finding of new targets a high-risk approach, which is very time-consuming, requires single-agent toxicity studies and high financial costs. Development of novel targets depends on early phase trials involving committed pharmaceutical company.

Prof. Higgin’s group identified that depletion of DNA polymerase theta (POLQ) induces tumor-specific radiosensitization. POLQ is a key player in the microhomology-mediated end-joining (MMEJ) pathway and is upregulated in multiple homologous recombination (HR)-deficient and HR-proficient cancers. As POLQ is an attractive therapeutic target, Prof. Higgins established a collaboration with Cancer Research Technology to develop inhibitors against this target.

2. Repurposing of established drugs used for other clinical indications - a low risk approach with well-established toxicity profile. There is no requirement of pharma approval for early phase trials. Thus, this approach bears limited opportunity to obtain meaningful intellectual property.

Prof. Higgins is investigating the efficacy of a widely used and well tolerated antimalarial drug Atovaquone. His laboratory’s finding was that Atovaquone reduces oxygen consumption in tumor cells, thereby decreasing tumor hypoxia, and increasing radiosensitivity.

Prof. Higgins also reported on the first ever UK clinical trial combining a ‘targeted’ PI3K inhibitor (BKM120) with radiotherapy in lung cancer patients. This study has recently been completed and appears to support the hypothesis that PI3K inhibition reduces tumor hypoxia.

Magdalena Staniszweska