May 07, 2019 - Prof. Dr. Marc Vooijs

Extraordinary Professor Department of Radiation Oncology
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‘Targeting the Therapeutic Ratio in cancers’

Marc Vooijs is a professor at the department of radiotherapy / Maastro Lab at the Maastricht University Medical Center (MUMC+). His research focuses on exploiting the tumor microenvironment and to improve combination treatments with radiotherapy in cancer. His research is based on mechanistic insights of signal transduction by NOTCH family proteins and their context-dependent role in cancer development and treatment response, with an emphasis on tumor microenvironment and hypoxia. Furthermore, he is developing new reagents to monitor the NOTCH activation cascade under normal and pathophysiological conditions.

His talk was focused on his research with the NOTCH signaling pathway. He reported about different synergistic drug combinations which are under investigations because of the need of new therapeutic targets. Those therapies are essential for diseases like T-cell Leukemia. Furthermore, he mentioned that stem cell pathways are often deregulated in cancers, like Wnt or NOTCH signaling pathways as well as molecules like p53. But if stem cell pathways are chosen as treatment targets, there is also an effect on normal tissue.

His group developed antibodies to bind to the active cleavage site of NOTCH. This leads to an accumulation of precursor products which in the end lead to a blockage of the whole pathway. In further investigations, they could see that NOTCH proteins are also found in different kinds of vesicles. Those can be targeted by changing pH values leading to reduced viability and increased levels in apoptosis. It is still not fully understood why NOTCH is found in vesicles. There are the possibilities that it is part of a recycling process, if a fully activation of NOTCH failed. But on the other hand, there is also active NOTCH found in vesicles. That leads to the question if cleaved NOTCH is the same as active NOTCH. Furthermore, the effect of chloroquine (CQ) and gamma secretase inhibitor (GSI) were investigated. GSI and CQ act synergistically to induce cell death in T -ALL and they want to find out how CQ affects T-ALL survival. CQ leads to an increase in G_0/G_1 and S phase levels. Moreover ROS levels were increased after treatment of CQ, GSI and its combination. CQ shows also other effects like its ability to bind to DNA, resulting in a DNA damage response, even in the absence of damage. However there are also difficulties using CQ for treatment, because some patients develop resistances.

Alina Wittka and Christine Hansel