Exploring New Ways to Treat Uveal Melanoma

What is the Tumor Microenvironment?

The tumor microenvironment is the area around a tumor that affects how the cancer grows and responds to treatment. Important factors in this environment are oxygen levels, acidity (pH), blood flow, and metabolism.

Why Study Uveal Melanoma?

Uveal melanoma (UM) is a rare eye cancer, and despite the high effectiveness of treatment of the primary tumor, it causes high mortality in patients with metastases. This is due to its high resistance to chemo and immunotherapies. Little is known about the uveal melanoma microenvironment and its role in response to therapies. The search for mechanisms underlying the resistance of uveal melanoma is important for understanding its biology and development, and in the future may contribute to modifying treatment methods. In a human UM model in immunocompromised mice, we will examine how radiation modulates the physiological parameters of the tumor. In the project, we plan to implement the treatment of tumors with verterporfin. We postulate that it may affect the tumor microenvironment and change parameters such as oxygen partial pressure, pH, functional vascularization and inorganic phosphate concentration.

How Does Verteporfin Help?

Verterporfin is known to delay the growth of UM cells. It may work by changing the tumor environment, affecting oxygen levels, pH, blood flow and metabolism. Changes in these parameters may lead to increased effectiveness of radiotherapy.

Monitoring the Tumor Environment

We will use special techniques to study changes in the tumor microenvironment:

- Electron Paramagnetic Resonance (EPR): A non-invasive way to measure changes in the tumor microenvironment.
- Rapid Scan: A new method for fast and detailed 3D imaging.
- Ultrasound Imaging: To visualize tumor growth and its blood vessels.
- Immunohistochemical staining: To check for markers related to cancer spread, stress, metabolism, and blood vessels.

Research Goals

Our main goal is to see if verteporfin makes the tumor environment more sensitive to radiation. We plan to:

1. Improve imaging methods using Rapid Scan.
2. Use ultrasound to study tumors and their blood vessels.
3. Measure oxidation, pH, and metabolism in living mice.
4. Study how verteporfin and radiation affect tumor blood vessels and metabolism.
5. Analyze all the data together to understand the effects better.

Innovative elements of the proposed project include the use of a multifunctional HOPE spin probe, which can simultaneously determine the oxygen partial pressure, pH and the concentration of inorganic phosphate in tissues. Rapid Scan technique has not been used so far in the context of in vivo applications. Only the recent construction of equipment allows this research path to be developed. The third element of innovation is the use of verteporfin in combination with radiation. Despite the ambitious research plan, we are convinced that the qualifications and experience of the team as well as the availability of advanced methods guarantee the achievement of the intended goals.