



Towards the prediction of therapy response for renal cell cancer

Researchers find relevant biomarkers for predicting and monitoring antiangiogenic therapy outcome for a subtype of renal cell carcinoma in mice. To achieve so, the team used non-invasive diffuse optical techniques.

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Clear cell renal cell carcinoma (ccRCC), characterized by its high metastasis and mortality rates, is the most prevalent subtype of renal cell carcinoma, one of the most common urinary cancers. An approach aimed at treating this kind of tumors is based on antiangiogenic drugs, that is, treatments that inhibit blood vessels formation, thus reducing nutrients and oxygen supply and, consequently, preventing further tumor growth.

The standard first-line antiangiogenic treatment is called **sunitinib**. Despite being the first option in many cases, almost 30% of patients present intrinsic resistance to it or acquire resistance within the 6th to the 15th month of therapy. Choosing an ineffective treatment not only is time and energy consuming, but also can worsen cancer aggressiveness. Thus, having tools to ascertain the right diagnostic is of huge importance. While extracting predictive

biomarkers of therapy resistance and response could help clinicians discriminate which patients would benefit from treatment, to date a non-invasive and practical alternative is still lacking.

ICFO researchers from the **Medical Optics group** led by **ICREA Prof. Turgut Durduran**, in collaboration the Tumor Angiogenesis group of ICO-IDIBELL led by Dr. Oriol Casanova, have obtained promising results in this regard, having recently appeared in Biomedical Optics Express. By applying diffuse optical techniques in a ccRCC mouse model, the team has found significant biomarkers to predict the response to sunitinib treatment, both before and during therapy.

These techniques give information about the microvascular hemodynamics in a **safe, non-invasive and practical way**, and have already been tested on humans for other purposes. Therefore, moving from mice to humans should be feasible, researchers say. That could be a path to follow, since **the results suggest that diffuse optical techniques are a suitable toolbox for predicting the therapeutic resistance of a ccRCC tumor to antiangiogenic therapy before administrating the drug and throughout the treatment.**

Towards validated biomarkers for clear cell renal cell carcinoma

In the reported experiment, some mice's tumors were treated with sunitinib and compared to the control group, where no antiangiogenic treatment was applied. Among those under sunitinib treatment, some of them responded positively and some others did not, similarly to what happens in the clinics.

Researchers applied diffuse optical techniques (diffuse correlation spectroscopy and diffuse reflection spectroscopy) to all of them and then compared the outcomes between groups. In particular, they measured three parameters: blood flow index, total hemoglobin concentration and blood oxygen saturation.

After collecting the data, researchers found that total hemoglobin concentration and specially blood flow index were potential biomarkers to determine whether the animal was inherently resistant to sunitinib before treatment. For instance, higher values of blood flow index correlated with higher chances of being resistant to sunitinib.

Moreover, they monitored in real-time the three parameters during the whole treatment protocol, and saw clear differences between therapeutic and control groups. That showcased the suitability of diffuse optical methods as tools for assessing and linking hemodynamics changes to therapeutic effects during treatment.

The provided biomarkers might allow for an early identification of intrinsic or developed resistance of these tumors to sunitinib. In turn, **this could help medical professionals make more informed and individualized decisions on which drug administer to a given patient, improving therapy effects, efficiency and even avoiding worsening the disease prospects.**

Reference:

Miguel Mireles, Gabriela Jimenez-Valerio, Jordi Morales-Dalmau, Johannes D. Johansson, Mar Martinez-Lozano, Ernesto E. Vidal-Rosas, Valenti Navarro-Perez, David R. Busch, Oriol Casanovas, Turgut Durduran, and Clara Vilches, "Prediction of the response to antiangiogenic sunitinib therapy by non-invasive hybrid diffuse optics in renal cell carcinoma", *Biomed. Opt. Express* 15, 5773-5789 (2024)

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