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## Immuno-oncology on chip: recreating and measuring heterogenous cell battling in tumor ecosystem.

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The immune system is a striking example of an integrated information system, engaged in coordinated host-protective activities. The heterogeneity of immune infiltrate in tumors is now well recognized as an emerging determinant of the efficacy of the anticancer therapy and can be harnessed to patients' benefit.

Fundamental cancer research and the development of efficacious antineoplastic treatments may take advantage of significant advanced screening human biology-based in-vitro models and computational tools providing detailed morphological and functional insight into living cells. While in vivo studies function as a gold standard, tissue-engineered micro-physiological tumor models can offer patient-specific insights into cancer-immune interactions, measured in a relevant physiological context, allowing both real time manipulations and functional readouts. Combining microfluidics with the ability of cellular imaging enable to collect quantitative data from complex biological systems at a single-cell level, we present our approach to create an active human-based organs-on-chip ecosystem relevant to immune-oncology, allowing to visualize and measure immune contexture in tumors in automated and in a controllable fashion. Different experimental setups allowed to describe a wide range of scenarios to study the effects of immunomodulatory drugs, genetic modifications and the role of stroma components in chemo- or immune- therapies regimes in heterogeneous tumor-immune microenvironments, consistent with in vivo observations.

All our results indicate not only the efficacy of the microfluidic based coculture approach, but also show, in our opinion, as organs on chip represent a bridge connecting biology and mathematical models, with piers resting on advanced microscopy and data analysis, but still need to be integrated with other disciplines such as systems biology and agent based models.

**Short Bio:** Negli ultimi 20 anni, Luca Businaro ha sempre lavorato all'applicazione di tecniche di fabbricazione top-down a diversi settori della ricerca di base ed applicata, con particolare riguardo alla fotonica, alle ottiche per raggi X ed alla microfluidica finalizzata alle applicazioni biomediche. Dal 2010 si e' trasferito a CNR-IFN Roma, dove ha continuato ad interessarsi di micro e nano fabbricazione per la nanofotonica e la microfluidica. In particolare, si e' appassionato all'utilizzo dell'approccio Organo su Chip per cercare di modellizzare e studiare sistemi biologici complessi, soprattutto l'interazione tra sistema immunitario e malattie. Da gennaio 2021 fa parte della famiglia CNR-NANOTEC con l'idea di potenziare le attività di organi su chip per lo studio del sistema immunitario e oltre.

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