Consiglio Nazionale delle Ricerche
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"Incontri al DSB"

STAT3 and beyond at the cross road between inflammation, cancer and cancer stroma

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Online webinar

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STAT3 is a pro-oncogenic transcription factor that is activated downstream of a plethora of cytokines, growth factors and inflammatory signals and whose activity is crucial both for the pathogenesis of auto-immune diseases and in the process of tumor transformation and progression, where it affects the activity of both tumor and stroma cells.

We have demonstrated that STAT3 activity is both necessary and sufficient for the development of auto-immune myocarditis in mice, due to the amplification of an IL6-STAT3 feed forward loop in the liver. Indeed, we were able to cure myocarditis treating systemically with a liver-targeted siRNA against STAT3, raising several important questions related to the role of non-immune organs such as the liver in auto-immunity.

Digging into the role of STAT3 in mediating the cross-talk between tumor and stroma, we demonstrated that its activity is essential to endow Cancer Associated Fibroblasts (CAFs) with pro-tumoral activities. We identified a STAT3-driven signature in BC CAFs, conserved in patients and correlating with prognosis, of which several genes encode for secreted factors responsible for the stroma-to-tumor cross-talk in breast cancer, which can be readily accessed by inhibitors to impair primary tumor growth and metastases.

Finally, by analyzing gene co-expression patterns in vast BC databases, we identified gene modules correlated with prognosis amenable to disruption via interference with their hubs as a therapeutic approach.

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