Molecular basis linking chemoresistance and immunoresistance in differentiated and tumor-derived stem cells: innovative multitarget approaches

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The major limitation to the efficacy of chemotherapy is multidrug resistance (MDR), a multiple cross-resistance towards different anticancer drugs. Finding out new strategies against MDR may prevent and/or reverse the resistance to conventional chemotherapeutic agents and new anti-cancer targeted therapies. Beside killing MDR cells with the highest selectivity, the successful eradication of a drug-resistant tumor depends on the ability of chemotherapy to induce an immunogenic cell death, i.e. making tumor cells detectable by the immune system.

Our team found that:

1) MDR cells are also resistant to immune system;
2) the bases of the chemo-resistant phenotype rely on metabolic abnormalities (e.g. altered lipid metabolism, altered mitochondrial metabolism), which determine chemoresistance and atypical tumor-immune system interaction;
3) selective therapies targeting these metabolic abnormalities can restore chemo-immunosensititivity in MDR cells.

Our future goals and interests are to:

1) to create a collection of chemo-immunosensitive and chemo-immunoresistant cancer cells from different tumor models, including cancer stem cells;
2) to investigate the molecular and metabolic basis of the chemo-immunoresistant phenotype, in order to identify new therapeutic targets and diagnostic markers, in particular in cancer stem cells;
3) to validate new *ad hoc* adjuvant compounds, able to simultaneously induce chemo- and immunosensitization in resistant cells and cancer stem cells.

We are deeply interested in collaborating with researchers studying cancer metabolism and cancer stem cells.

Keykowrds: chemoresistance; immunoresistance; cancer metabolism; cancer stem cells

References

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