Lunedì 12 giugno 2017 alle ore 15.00

Sale Didattiche ex-sezioni di Patologia - Plesso Biotecnologico Integrato di Via Volturno

Saverio Tardito

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Rethinking glutamine addiction of glioblastoma

A defining hallmark of cancer is uncontrolled growth. This is initiated by alterations in signaling pathways that rewire metabolic homeostasis of cancer cells to sustain their increased energetic and anabolic demands. How these metabolic requirements are satisfied, depends in part, by the tissue of origin, which shapes the microenvironment, and determines the availability of nutrients for the tumor.
In accordance with its pleiotropic functions, glutamine is the most abundant circulating amino acid in humans, and in culture is the second most consumed nutrient by cancer cells. Glutamine-derived glutamate can be converted into α-ketoglutarate, which replenishes the tricarboxylic acid cycle metabolites, i.e. anaplerosis. On these bases, glutaminase, which favors anaplerosis by converting glutamine to glutamate, has been proposed as a therapeutic target for 'glutamine-addicted' tumors. However, the validity of this phenotype depends on the tissue of origin of the tumour. In glioblastoma, the most aggressive type of brain tumour, the glutaminase-dependent anaplerosis seems dispensable. Conversely, glutamine synthetase, which converts glutamate to glutamine, supplies the glutamine required for the *de novo* biosynthesis of nucleotide, and supports glioblastoma growth.

Saverio Tardito obtained his degree in Biology from the University of Parma in 2003. His PhD was carried out at the Dept. of Experimental Medicine of the University of Parma with Prof. Renata Franchi-Gazzola, and characterized the mechanism of action of metal-based compounds with cytotoxic activity against cancer cells. During his PhD Saverio gained interest in amino acids metabolism and studied the effect of a metabolic drug, asparaginase, in solid tumours, mentored by Prof. Ovidio Bussolati. In 2008 he was awarded a postdoctoral research fellowship from the Governement of Canada to join the group of Ian DeBelle at the Laval University, Quebec city, Canada, where he studied a non-apoptotic form of cell death. In 2009, Saverio returned to the University of Parma and in collaboration with Prof. Luciano Marchió, Dept. of General and Inorganic Chemistry, dissected the mechanism by which copper complexes induce non-apoptotic cell death in cancer cells.
In 2011, Saverio joined the lab of Prof. Eyal Gottlieb at the Cancer Research UK - Beatson Institute in Glasgow supported by an AIRC-Marie Curie postdoctoral fellowship. Here he focused on cancer metabolism, and in particular on the metabolism of glutamine in brain tumours. In 2016, Saverio was appointed jr Group Leader in the same Institute. Since then his Oncometabolism lab applies mass spectrometry-based metabolomics, cell biology, and biochemical approaches in advanced models of cancer to understand the tissue specific biochemical pathways that support tumour growth.