Curriculum Vitae: Tiziana Crepaldi

Tiziana Crepaldi graduated in Biological Sciences in 1980 and received a Ph.D. in Human Genetics in 1988 at the University of Turin, Italy. She worked as Research Fellow at the Dept of Oncology and Candiolo Cancer Institute, University of Turin (1989-2004), and the Curie Institute, Paris, France (1995). In 2005 she was appointed as Associate Professor in Biochemistry at the Dept of Oncology, University of Turin, Italy (2005-present).

Over the last three decades, Tiziana Crepaldi has investigated the molecular and cellular mechanisms that control the signaling of Hepatocyte Growth Factor (HGF) and Met tyrosine kinase receptor in development, tissue repair and cancer.

She published 68 papers and her Scopus *h*-index is 24.

She firstly reported (Prat et al., *Mol. Cell. Biol.* 1991) the C-terminal truncated forms of Met receptor, now well-known as "Met decoy" molecules, which interfere with both HGF binding to Met and Met homodimerization, and thus were subsequently exploited to inhibit Met in cancer. Then, she demonstrated (Crepaldi et al., *J. Cell Biol.* 1994) that the Met receptor is selectively exposed at the basolateral plasmamembrane domain of polarized epithelial cells. Next, she focused on membrane peripheral proteins able to convey the signals elicited by HGF receptor to the actin cytoskeleton machinery. She reported that Ezrin is critical for engagement of actin cytoskeleton in apical domain morphogenesis and cell migration promoted by HGF (Crepaldi et al., *J. Cell Biol.* 1997). She generated and characterized for the first time monoclonal antibodies (mAbs) directed against the extracellular domain of Met, able to behave as either full or partial agonists of Met (Prat et al., *J. Cell Sci.* 1998). One of these antibodies (DN30) was further characterized in the Paolo Comoglio's lab, deprived of agonistic activity and developed as a potent, selective, and irreversible inhibitor of ligand-dependent and ligand-independent Met activation.

She also discovered a new Met Interactor (Fap68) which is able to couple Met with p70S6K, by performing a genetic screen with the yeast two-hybrid system (Grisendi et al., *J. Biol. Chem.* 2001). By collaborating with Carola Ponzetto, she discovered that Met also contributes to the embryonic development of hyoid arch-derived facial muscles (Prunotto et al., *Dev. Dyn.* 2004). She also helped starting a new approach to inhibit Met through siRNAs, which are useful to suppress Met-mediated transformation in cancer (Taulli et al., *Cancer Gene Ther.* 2005). In collaboration with Aldo Fasolo, she showed that HGF regulates migration of GnRH (Giacobini et al., *J Neurosci*. 2007) and olfactory neuron precursors (Garzotto et al., *J Neurosci.* 2008). Then, by using the tetracycline-dependent regulatory (tet-off) system, she generated transgenic mice with inducible targeted expression of either Met or HGF in skeletal and cardiac muscle (Crepaldi et al., *J. Biol. Chem.* 2007; Riess et al., *Trans. Res.* 2011; Leo et al., *Plos One* 2011; Sala et al., *J. Mol. Cell. Cardiol*., 2016; Morena et al., *ELife* 2016). These animal models provided powerful tools for assessing the effect of an extra-dose of HGF or activated Met in muscle tissues under physiological and pathological conditions. More recently, she exploited the Met agonistic mAbs as deliverable drugs that can substitute HGF in tissue repair and protection against injury (Gallo et al., *Cell Death Dis.,* 2014; Gallo et al., *Br J. Pharm*., in press).

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