Role of P2X7 receptor in immune response and extracellular ATP modulation during oncogenesis

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Extracellular ATP (eATP) is a major constituent of tumor microenvironment modulating cell growth, progression, anti-tumoral immune response and tumour host-interactions, including vessel formation and immune-cancer cell crosstalk (Di Virgilio et al., 2017). P2X7 receptor is an ATP gated ion channel which is recognized as a mediator of ATP activity in oncogenesis and it is involved in cancer cell proliferation, vascularization, migration and metastatization (Adinolfi et al., 2012; Jelassi et al., 2011, De Marchi et al., 2016). Moreover, it is well known the activity of this receptor to mediate immune cell activation leading to the vesicular release of proinflammatory cytokines such as IL-1β (Pizzirani et al., 2007; Gulinelli et al., 2012). We have also demonstrated that P2X7 blocking drugs act, in vivo, as efficacious anti-tumoral agents in different murine models (Adinolfi et al., 2012, Adinolfi et al., 2015, Amoroso et al., 2015). Here we analyzed the effect of P2X7 on eATP and immune response modulation in tumoral microenvironment. The role of P2X7 in ATP secretion has been explored thanks to a luciferase probe detecting eATP (PmeLUC), which was engineered to be expressed on the outer facet of the plasma membrane and emits photons in an ATP dependent-manner (Pellegatti et al., 2005, Pellegatti et al., 2008). The effect of P2X7 antagonist administration on eATP was evaluated both in vitro and in vivo in P2X7 wild-type and null mice. Interestingly, host P2X7 receptor was able to modulate tumoral levels of eATP. Data suggest that the alteration of eATP could be dependent upon microvesicles release of nucleotide by both tumor and host immune cells. Taken together we suggest an involvement of P2X7 receptor in eATP production during oncogenesis thus affecting tumor microenvironment.

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