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Survivin and cancer immunotherapy

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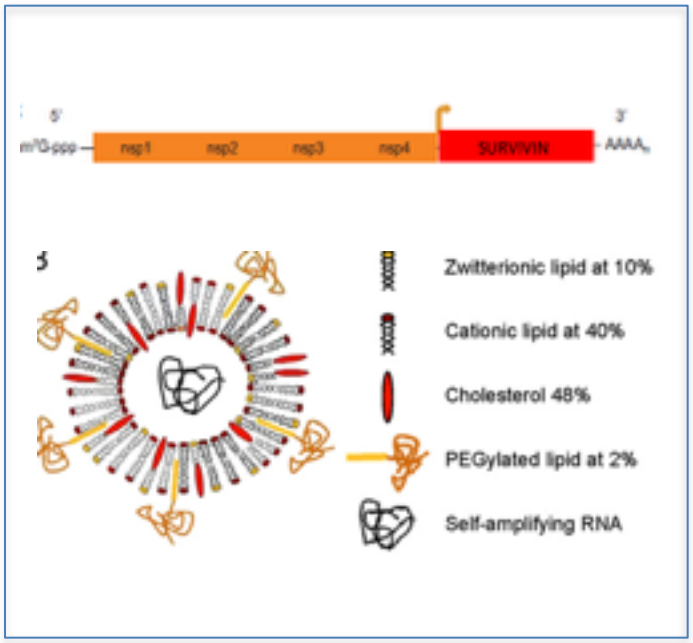

Survivin is a member of the inhibitors of apoptosis protein (IAP) family, implicated in regulation of mitosis, cell cycle and apoptosis. It is undetectable in most adult tissues but it is over-expressed in the majority of human cancers, and it is associated with metastasis and poor diagnosis. Moreover, oncologic patients sometimes show an immune response against Survivin. It seems that Survivin tolerance does not exist or it could be overtaken. These features make it an attractive therapeutic target. In particular, poxviral vaccines (MVA and FPV) have been tested in cancer mouse models. Despite positive results, viral vector approach presents some restrictions such as the immune response against the vector, delivery into the nucleus and possible DNA integration. To overcome these limitations, Novartis has recently developed the SAM (self-amplifying) RNA technology that presents some advantages because it induces higher gene expression, it is transiently expressed in the cytoplasm and it do not induce response against vector. The aim of my PhD project is to apply the SAM-RNA technology encoding Survivin in cancer mouse models, and to compare the immune response and protection induced by Survivin delivered as SAM-RNA or viral vectors.