## Myoferlin: an indispensable component in VEGF-A secretion by pancreas cancer cells

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Ferlin family proteins have been reported to participate in plasma membrane fusion, repair, and endocytosis concretely but not exclusively, it has been reported in skeletal muscle development and repair (myoferlin and dysferlin) and presynaptic transmission in the auditory system (otoferlin). While some reports have implicated a member of ferlin family proteins, myoferlin, in cancer; the extent of its expression in and contributions to cancer are not well established.

Myoferlin, a member of the ferlin protein family was recently identified in our laboratory as a new accessible biomarker for human pancreatic ductal adenocarcinoma. In addition to its potential suitability for targeted therapy, we aim to examine the biological role of this protein in the development of pancreatic cancer.

SiRNA-mediated myoferline-silencing significantly reduced the volume of BxPC-3 tumourstumors developed onto the chorioallantoic membrane of fertilized chicken eggs. Intriguingly, aside their reduced volume, myoferlin-silenced tumourstumors appeared whitish and exhibited a significant decrease of blood vessel density as shown by FITC-conjugated Sambuccus nigra agglutinin staining. This observation suggested that, in addition to an inhibition of BxPC-3 cell growth after myoferlin silencing, this protein may exhibit a pro-angiogenic activity. Accordingly, we next showed that myoferlin-silencing significantly inhibited VEGF-A secretion without decreasing VEGF-A gene expression. Western blotting and Immunofluorescence reveal that VEGF-A seemed to accumulate in the cytosol in the vicinity of the plasma membrane.

Knowing the previously reported role of myoferlin in membrane fusion processes, we proposed that myoferlin could play an important role in VEGF-A secretion by BxPC-3 cells. Currently, exocytosis and exosomes pathways have been explored showing, in BxPC-3 cells, that VEGF-A seems to be secreted by an alternative myoferlin-dependent pathway.