Role of myoferlin in mitochondrial dynamics and metabolic fitness of pancreas cancer

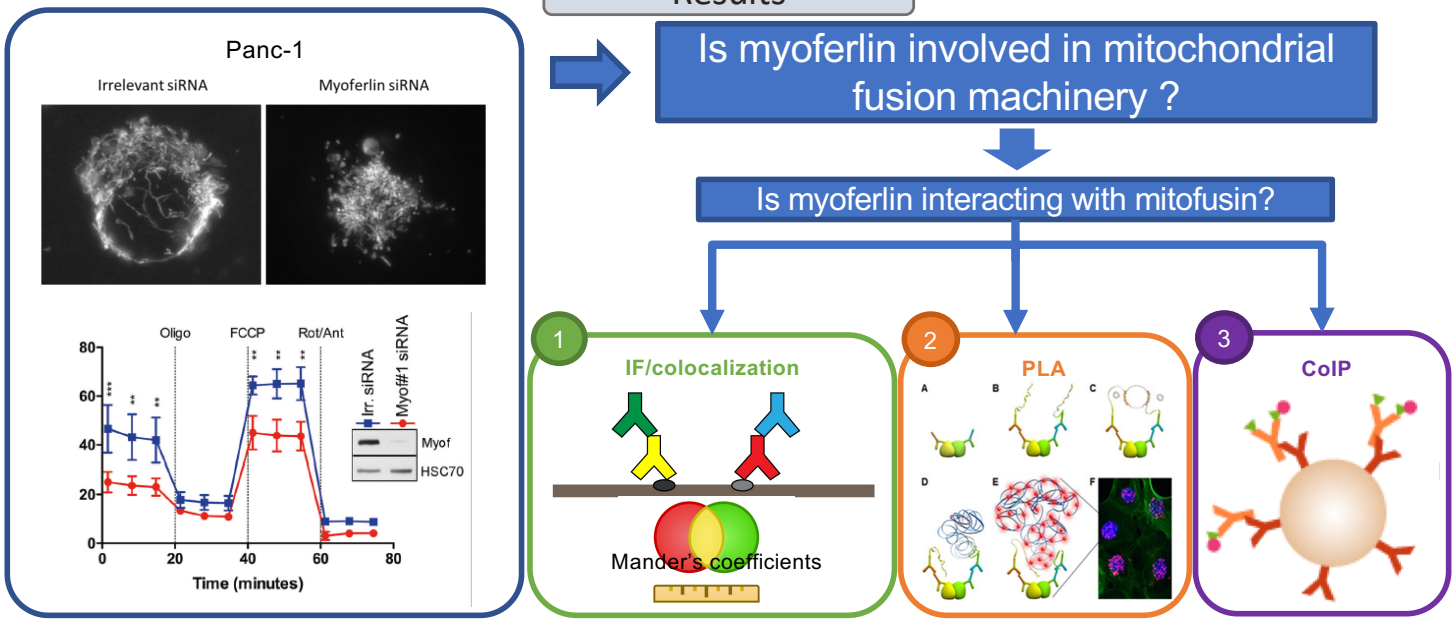
Sandy ANANIA, Gilles RADEMAKER, Raphaël PEIFFER, Alexandre HEGO, Louise DELDICQUE, Naima MALOUJAHMOUM, Ferman AGIRMAN, Akeila BELLAHCENE, Vincent CASTRONOVO, Olivier PEULEN

Mitochondrial Adaption in Cancer team
Metastasis Research Laboratory, ULiege

Introduction

Pancreatic cancer (PDAC) is the 7th most common cause of cancer mortality in the world. It is predicted to become the second leading cause of cancer-related death in 2030. Myoferlin is a 230 kDa protein overexpressed in pancreatic cancer. Recently, our team showed a fragmentation of the mitochondrial network in PDAC cells when myoferlin was depleted using siRNA. Understanding the mechanism underlying this mitochondrial disruption is of great interest as mitochondria are major actors in cancer development, progression and resistance.

Results



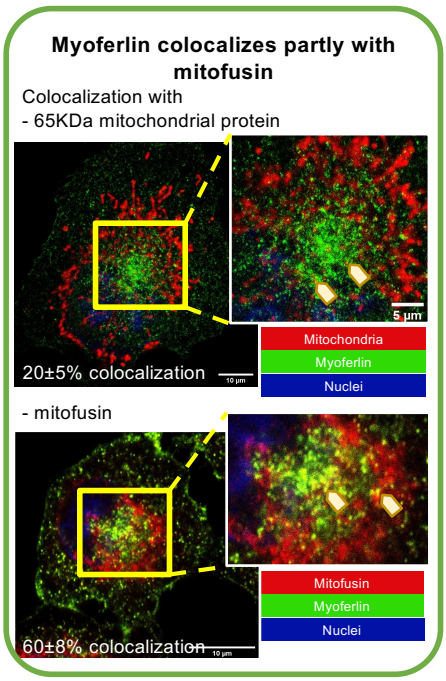


Figure 1: Myoferlin colocalization with mitochondria or mitofusin in Panc-1 cells. Mander's colocalization coefficient were calculated with ImageJ.

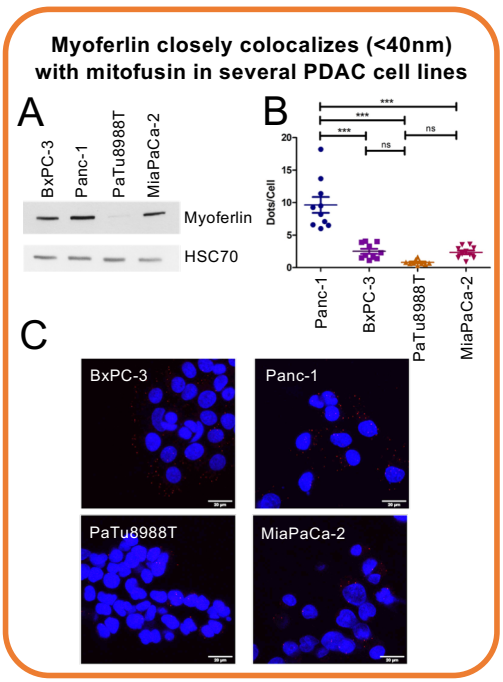


Figure 2: (A) Myoferlin abundance in PDAC cell lines. (B) Proximity assay quantification (colocalisation dots/cell). (C) Representative images of proximity ligation assay.

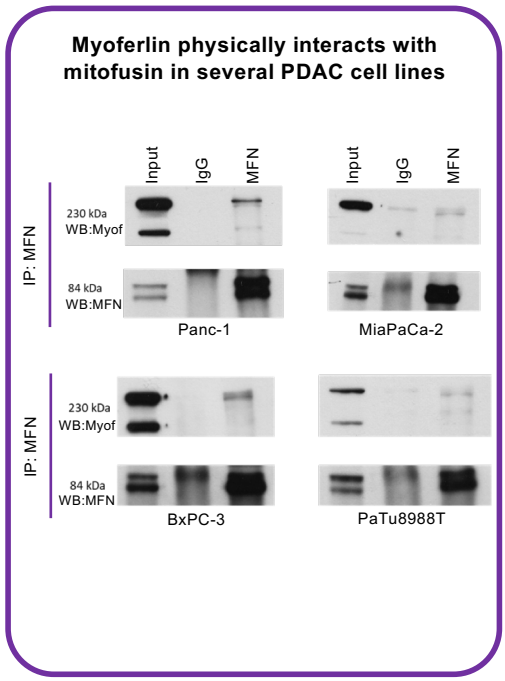


Figure 3: Myoferlin was co-immunoprecipitated with mitofusin (MFN) in several PDAC cell lines.

Recently, our team showed a mitochondrial fragmentation using siRNA targeting myoferlin. However, mechanisms underlying this process was still unclear. Our data strongly suggest that myoferlin interacts with mitofusin, a key actor of mitochondrial fusion machinery. This interaction could explain that myoferlin silencing, together with an unopposed fission, leads to mitochondrial fragmentation.

Sandy.Anania@uliege.be