



**Elisa  
Giovannetti**

**DEVELOPMENT OF  
BIOLUMINESCENT CHICK  
CHORIOALLANTOIC  
MEMBRANE (CAM)  
MODELS FROM PRIMARY  
PANCREATIC CANCER  
CELLS: A PLATFORM FOR  
DRUG TESTING**



**Cancer Pharmacology Lab**

*AIRC Start-up Unit Pisa*



**Medical Oncology  
Cancer Center Amsterdam**

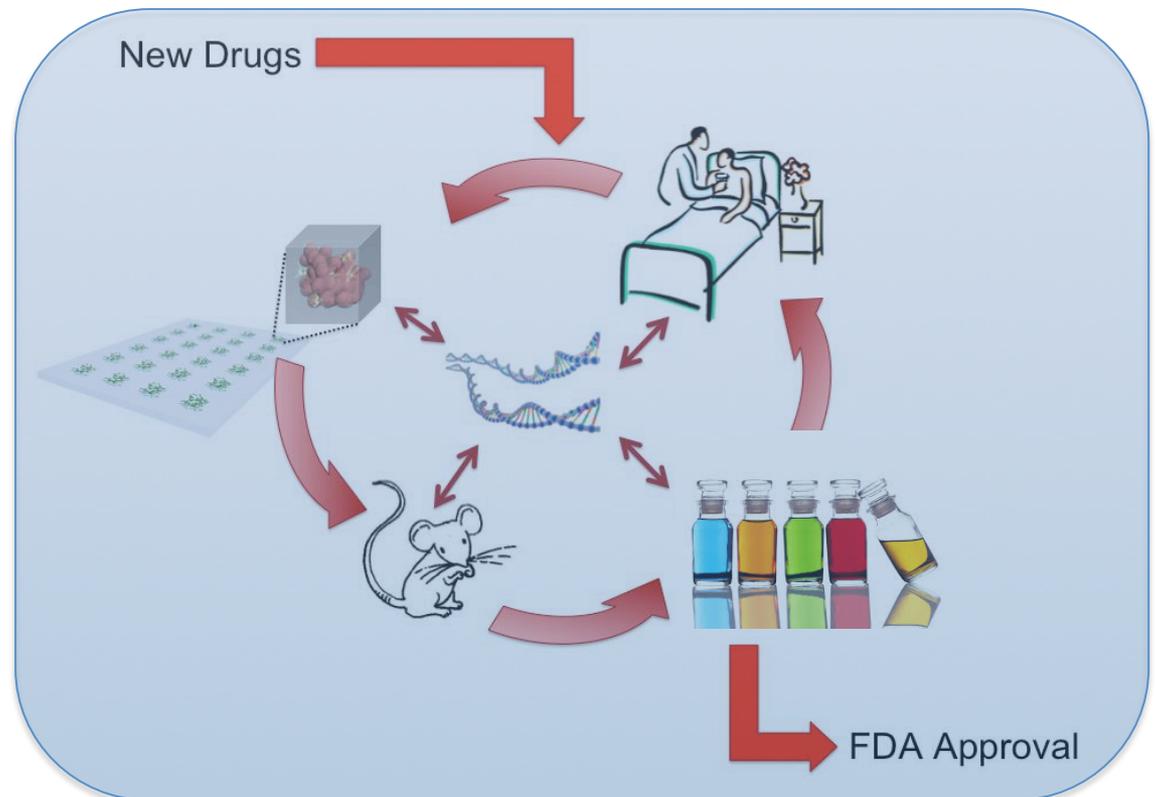
# Background

GEMMs, PDX/“avatar” mice and organoids have revolutionized

- the study of pivotal pathways in pancreatic tumorigenesis
- the identification of prognostic and predictive biomarkers

(*Olive et al., Science 2009; Aparicio et al., Nat Rev Cancer 2015; Giovannetti et al., JNCI 2014; Boj et al., Cell 2014*)

*Novel, cost-effective models that mimic tumor biology providing faster information on the activity of anticancer therapies could make a key contribution to the advancement of personalized medicine*

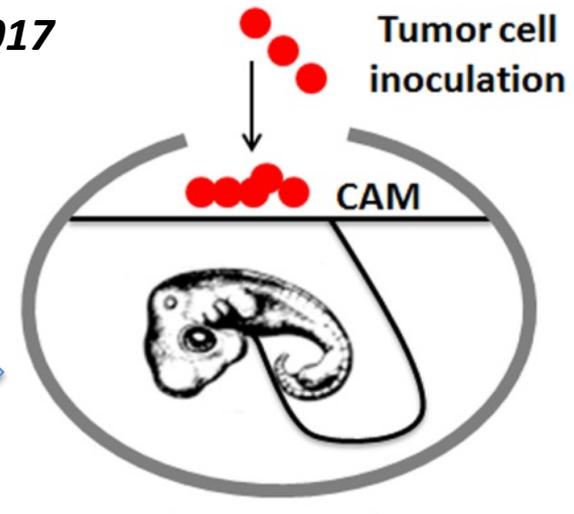
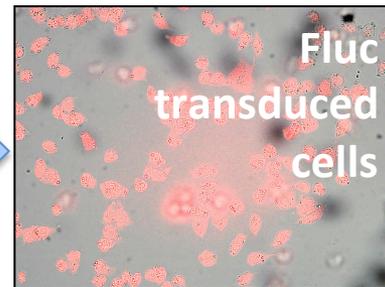


# AIM

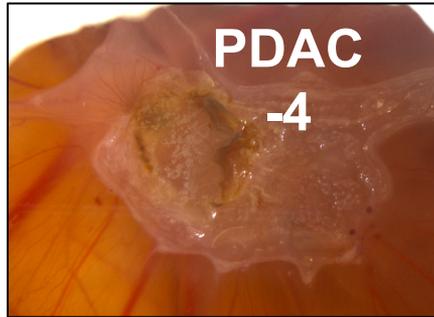
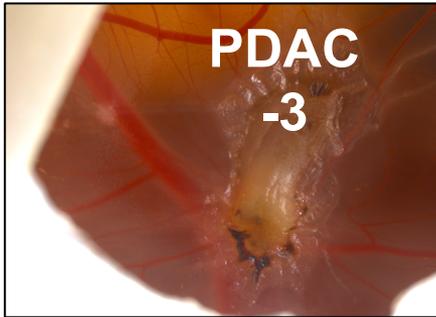
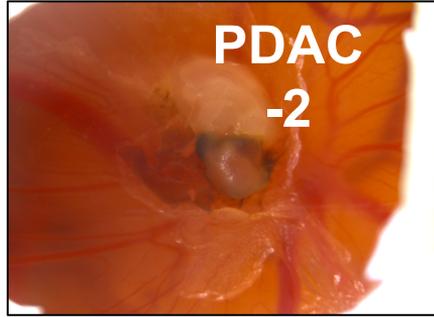
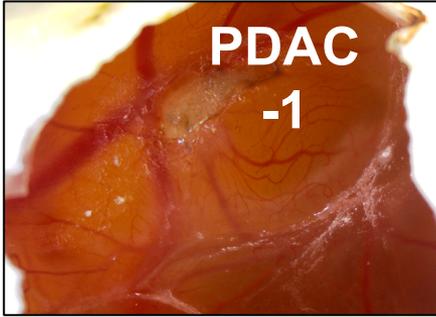
To develop chick-embryo chorioallantoic membrane (CAM) bioluminescent PDAC models for drug testing



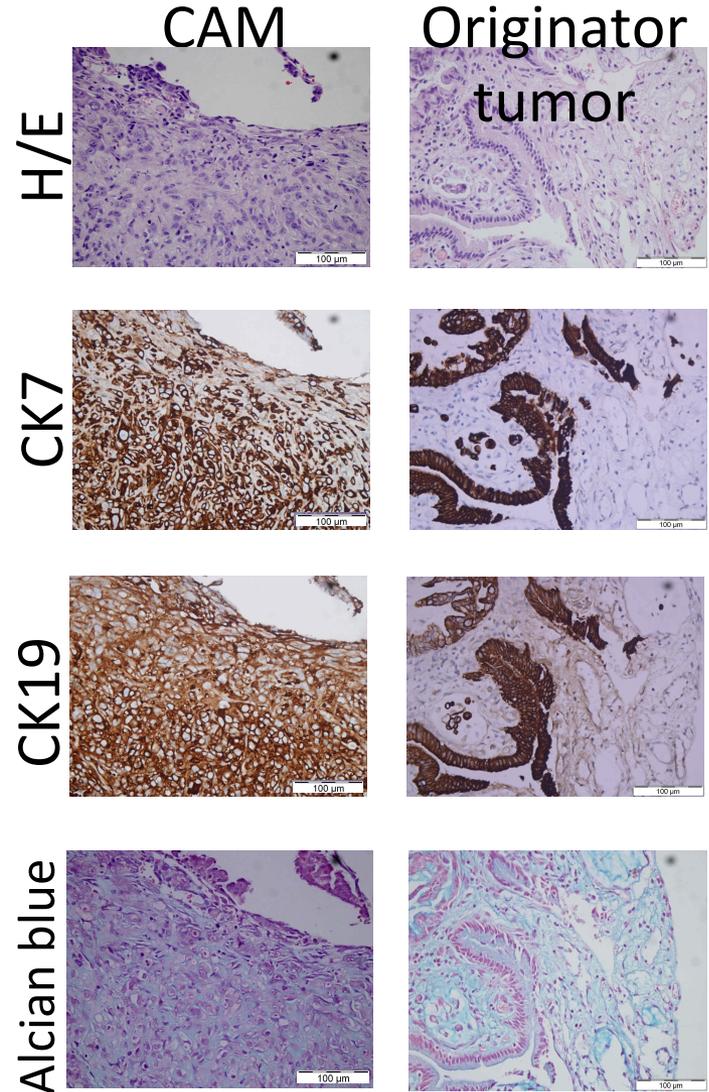
*Folkman et al, 1971*  
*Golan et al., BJC 2014*  
*Rovithi et al, Sci Rep 2017*



# Histopathological and IHC findings

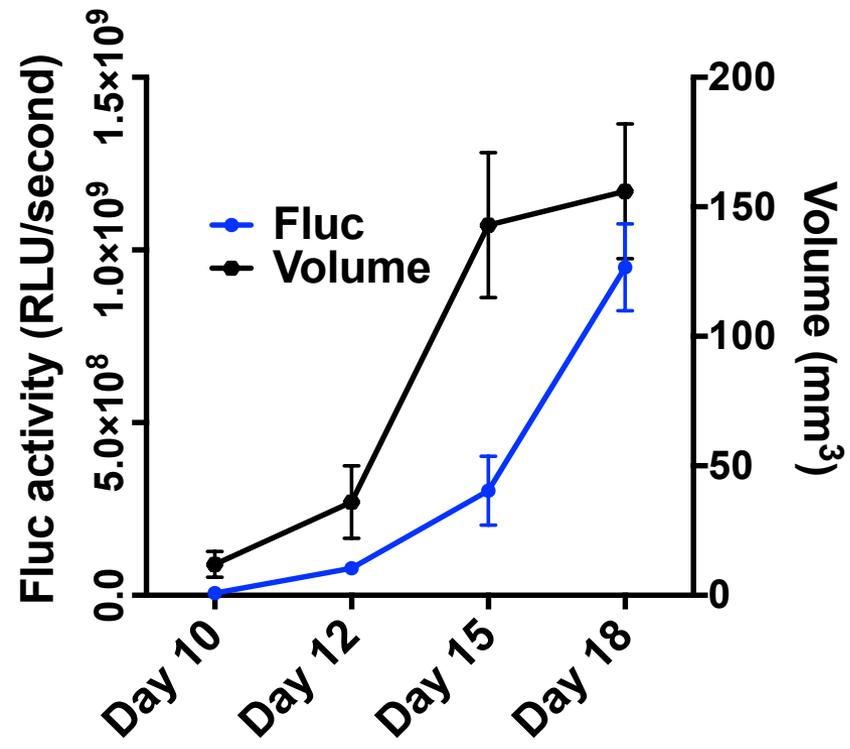
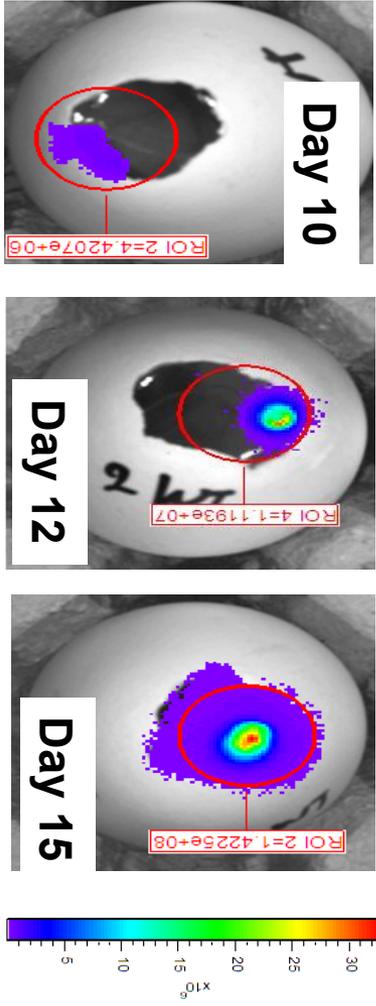


## PDAC-3 40X

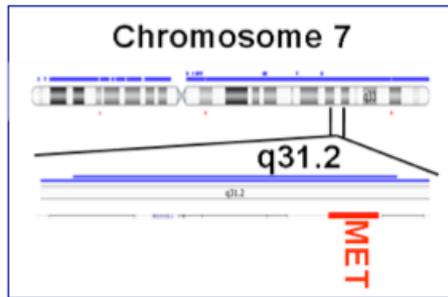




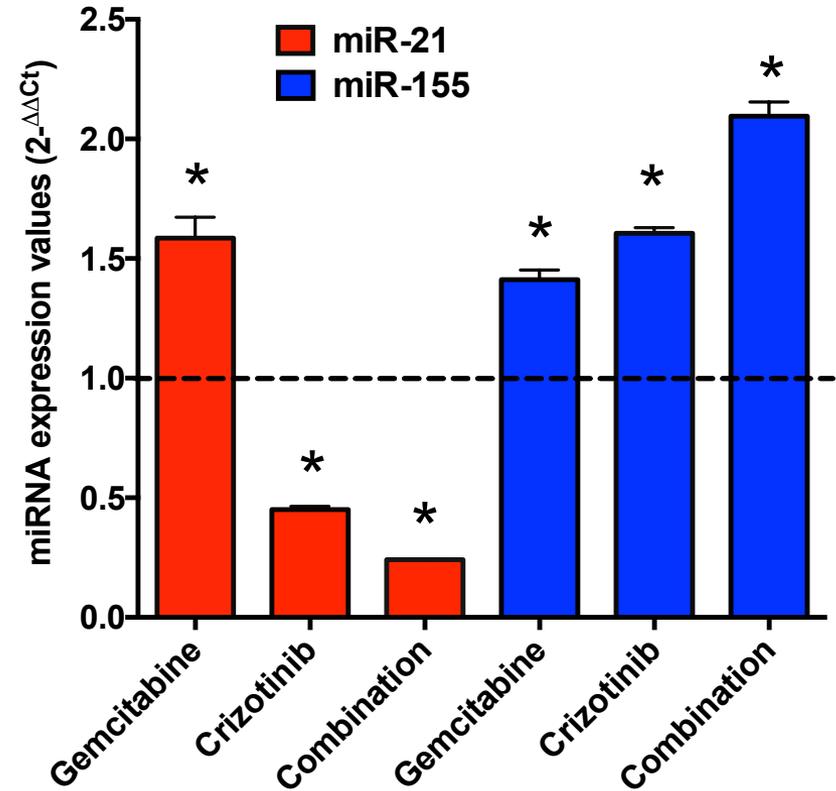
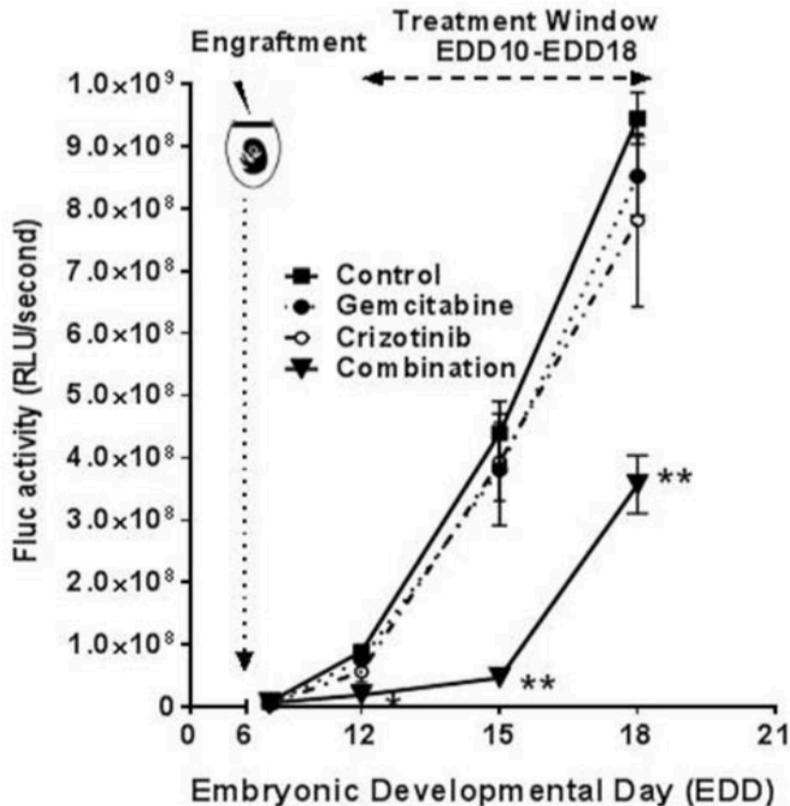
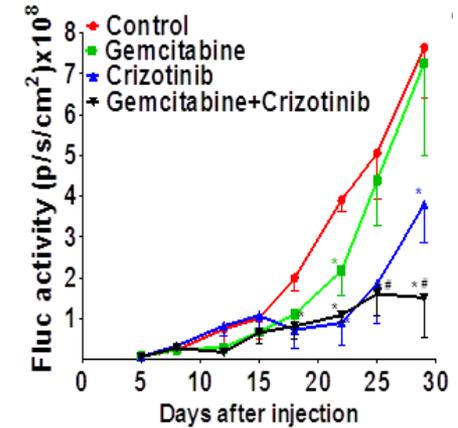
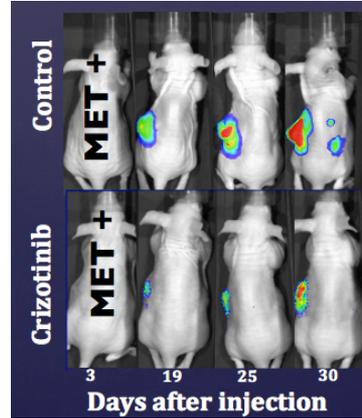
# Correlation of Fluc activity with tumor volume



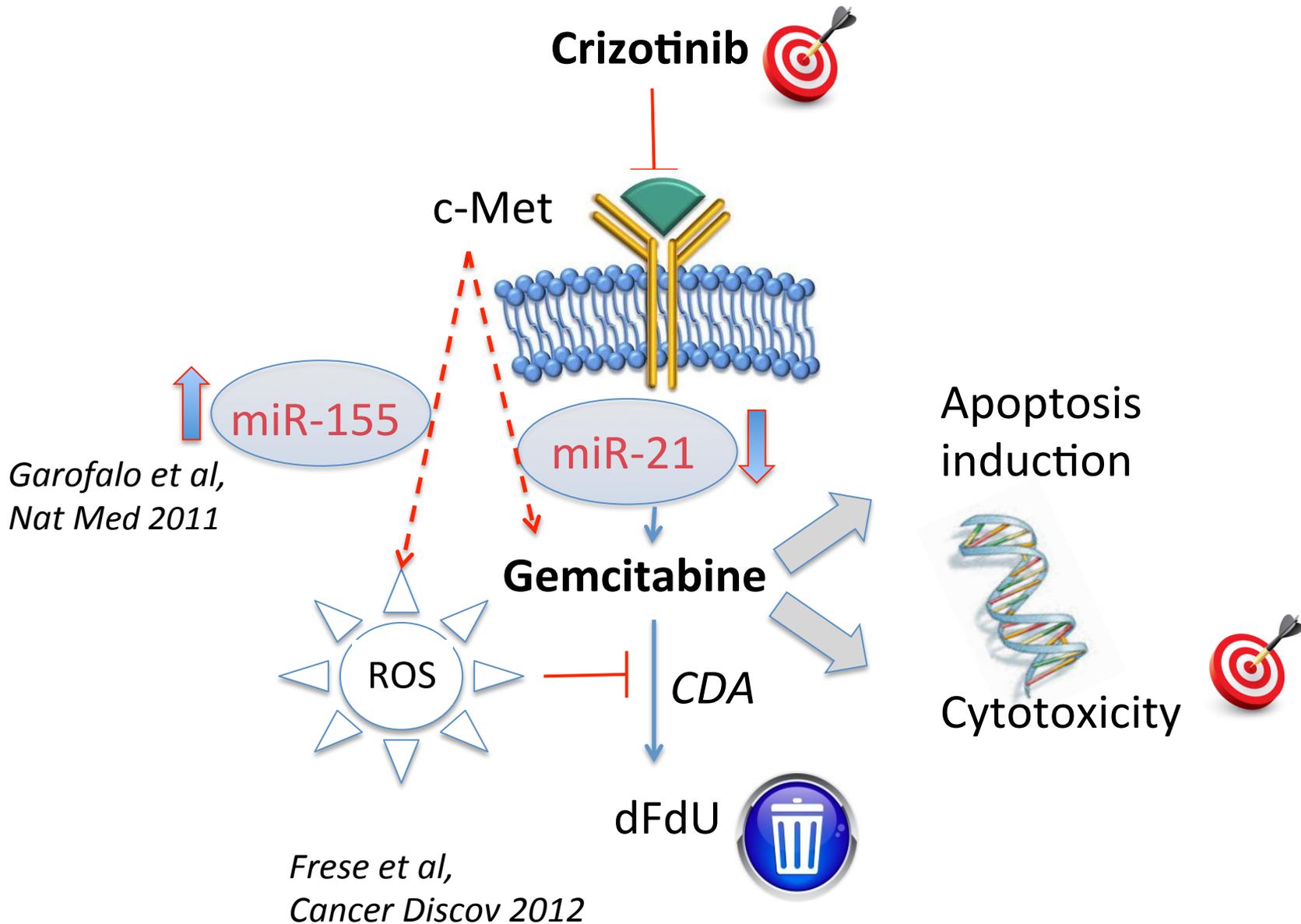
# A proof-of-concept study,... and something more



Avan et al, Cancer Res 2013



# A new hypothesis underlying synergism



# Conclusions

- Bioluminescent (Fluc) PDAC primary cultures were successfully inoculated onto the CAM membrane, with >80% engraftment.
- CAM tumors had histopathological miRNA profiles comparable to the original tumors
- One of these models was used to test the activity of gemcitabine and crizotinib, showing that combination treatment resulted in 63% inhibition of tumor growth ( $p < 0.01$  vs control)
- These results were associated with reduced expression of miR-21 and increased expression of miR-155, which might explain the synergistic interaction
- **CAM models of bioluminescent PDAC cultures represent an interesting preclinical platform, that could bridge the gap among monolayer cell cultures and more sophisticated in vitro and animal models**

# Acknowledgements



The Bennink Foundation

