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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**

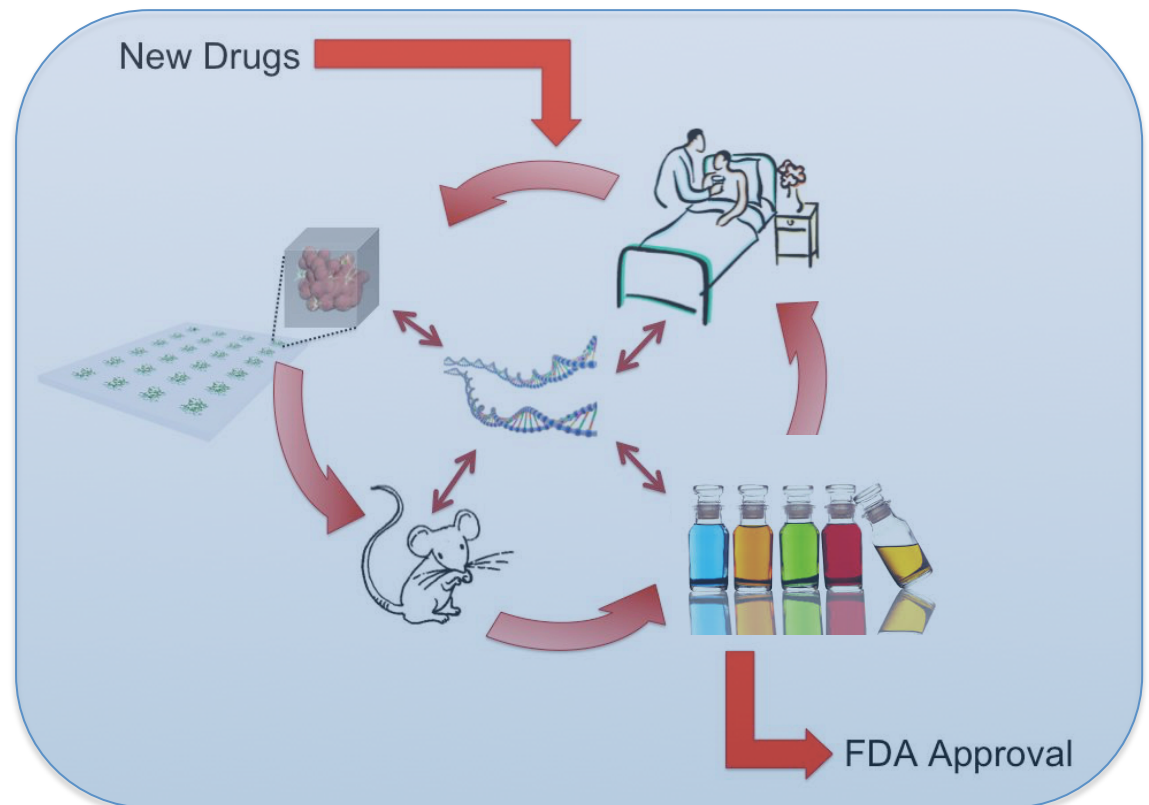
Background

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***

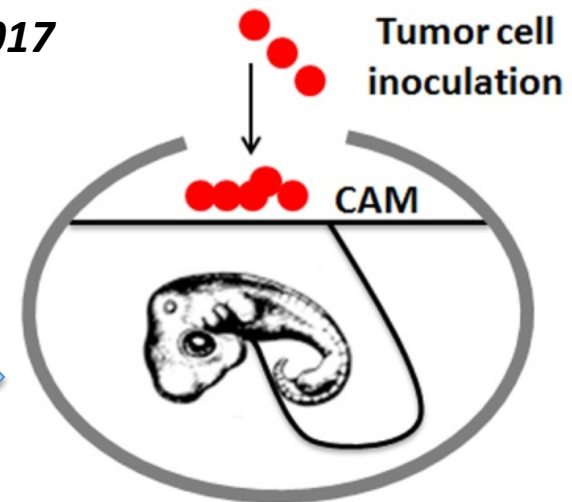
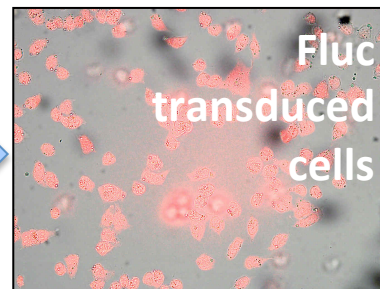


AIM

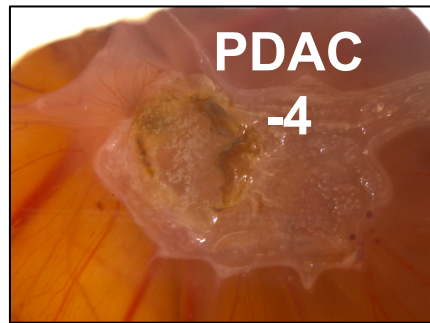
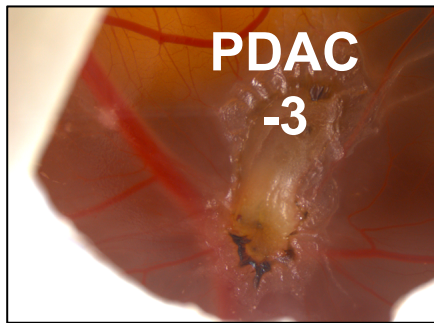
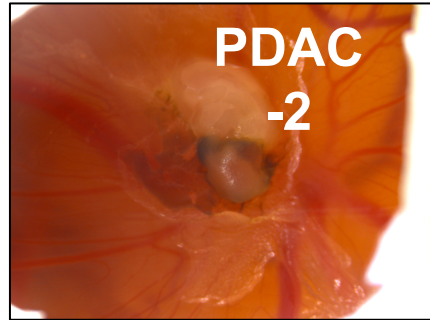
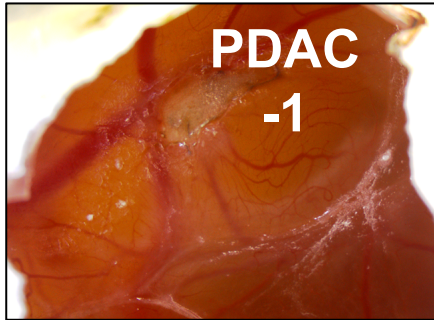
To develop chick-embryo
chorioallantoic membrane
(CAM) bioluminescent
PDAC models for drug
testing



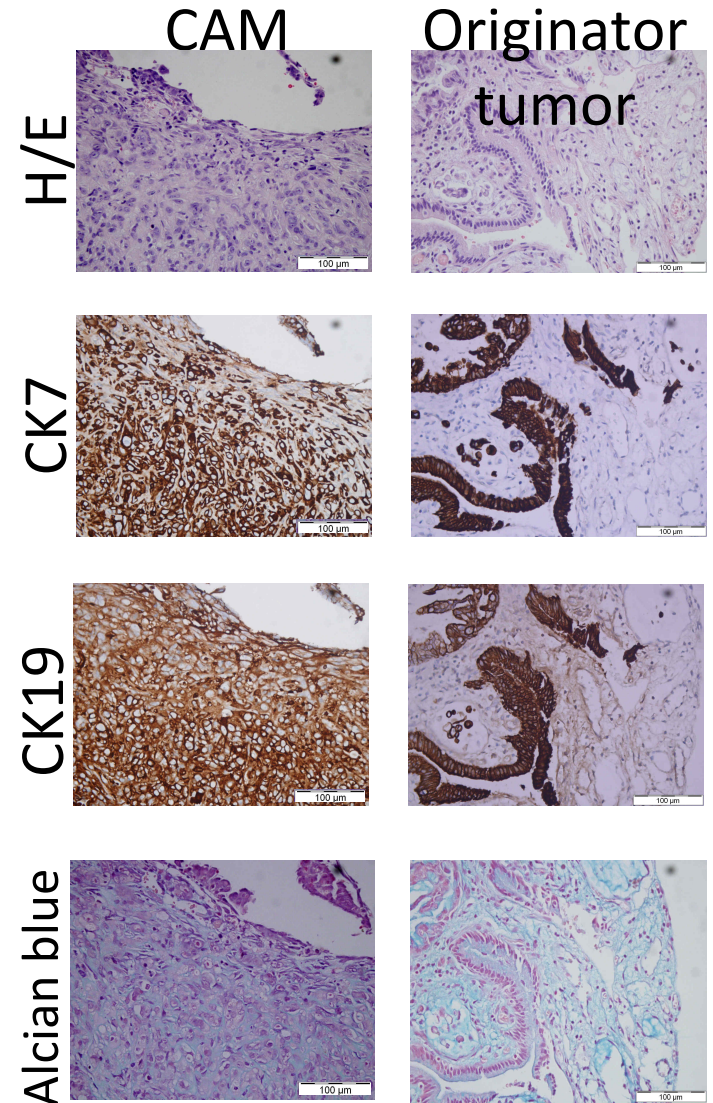
Folkman et al, 1971
Golan et al., BJC 2014
Rovithi et al, Sci Rep 2017



Histopathological and IHC findings

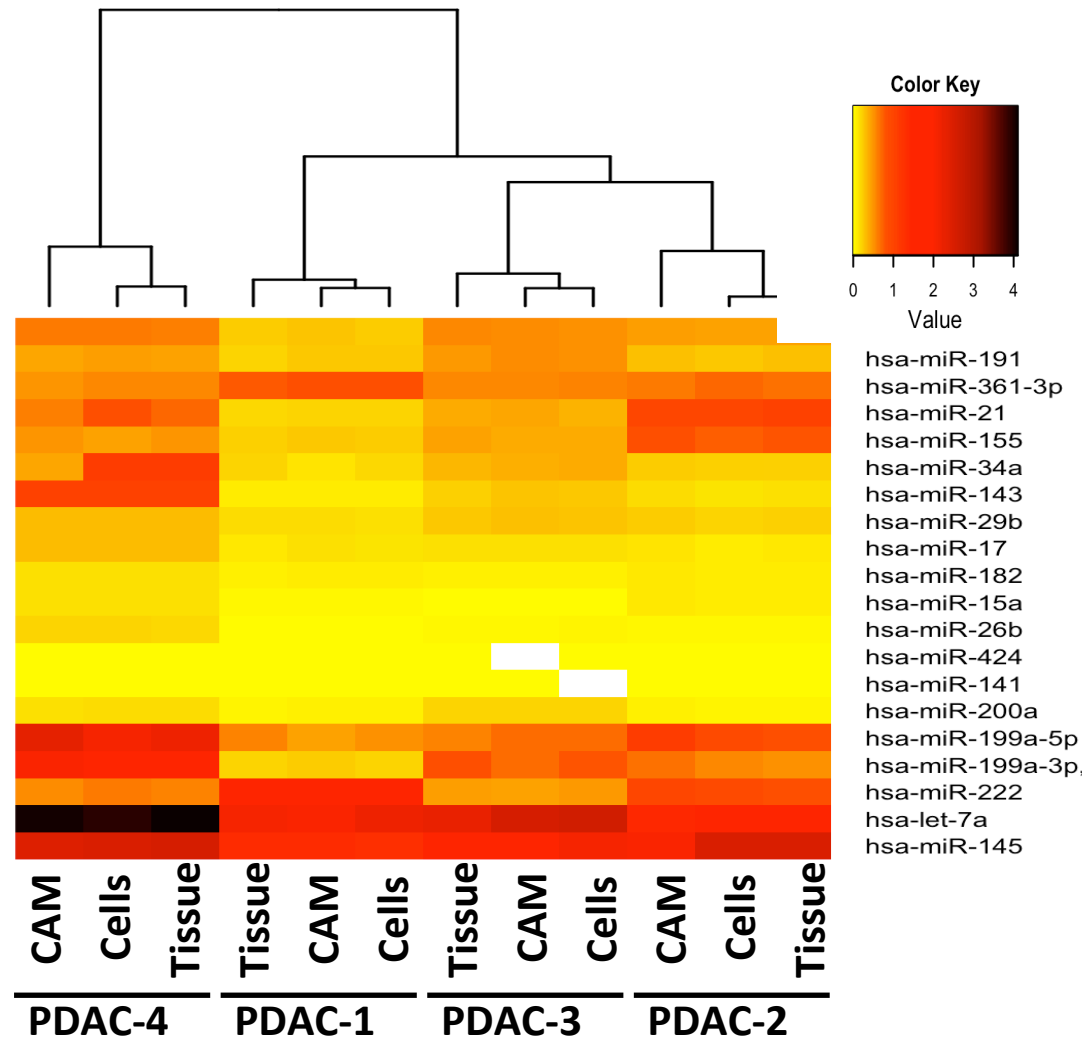


PDAC-3 40X

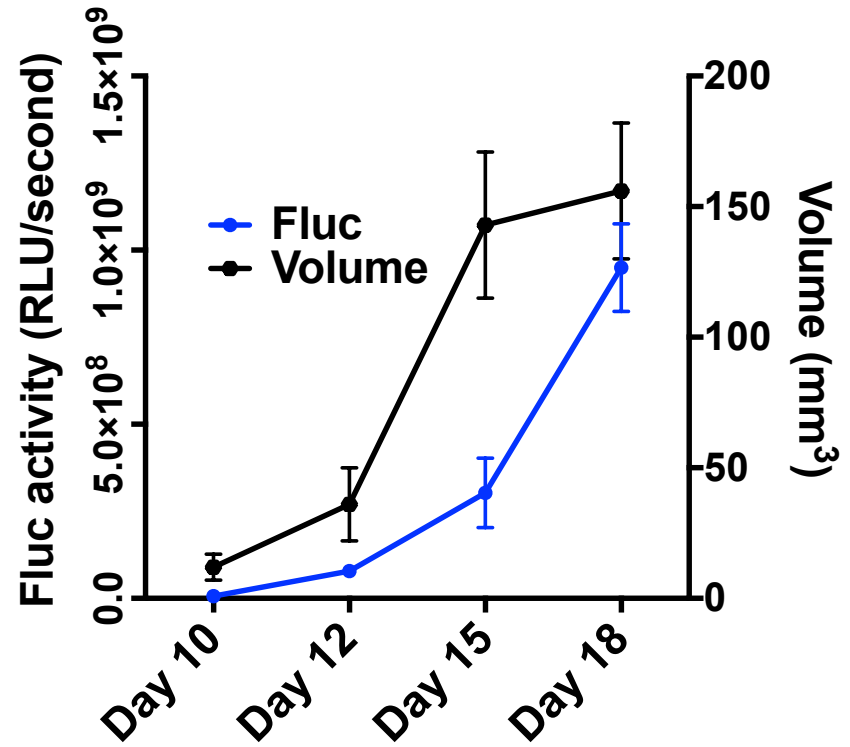
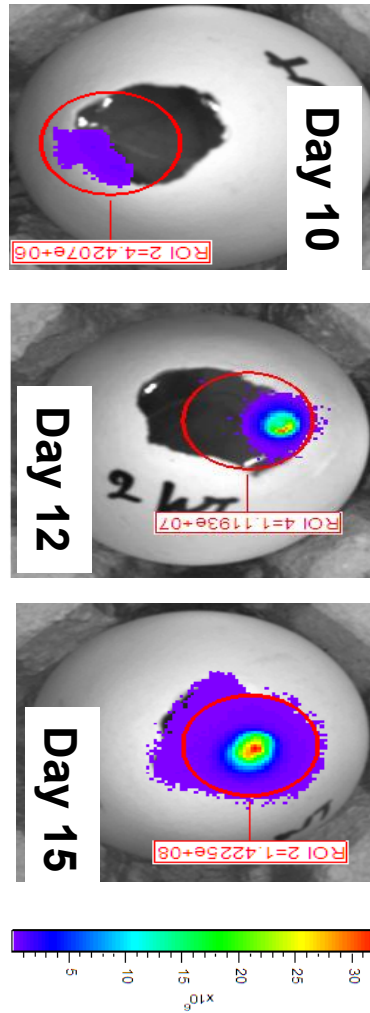


miRNA targeted profiling in CAM vs cells and tissues

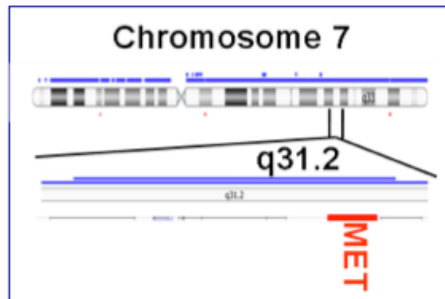
20 miRNAs selected from “A resource for analysis of microRNA expression and function in pancreatic ductal adenocarcinoma cells” Kent et al, 2009



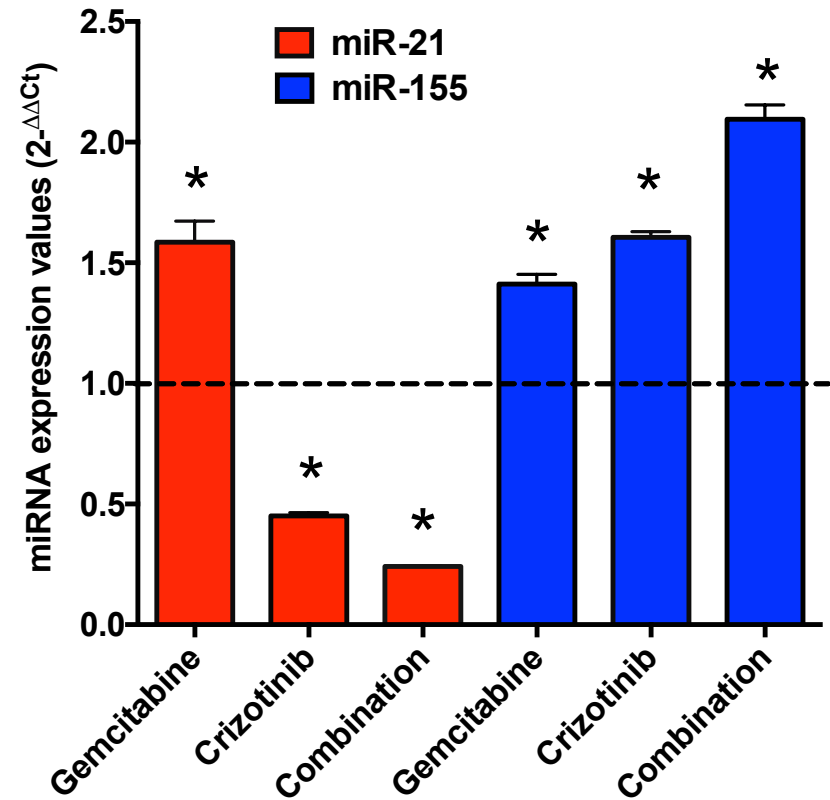
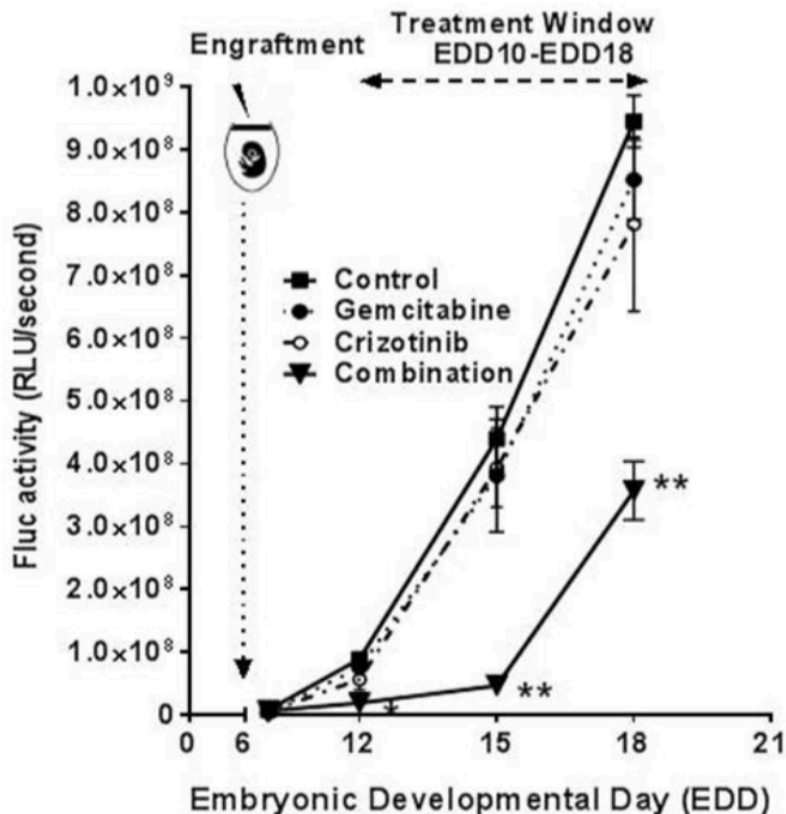
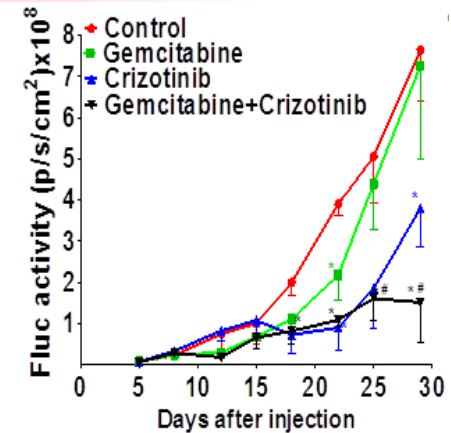
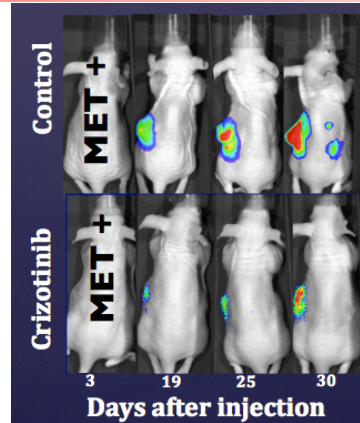
Correlation of Fluc activity with tumor volume



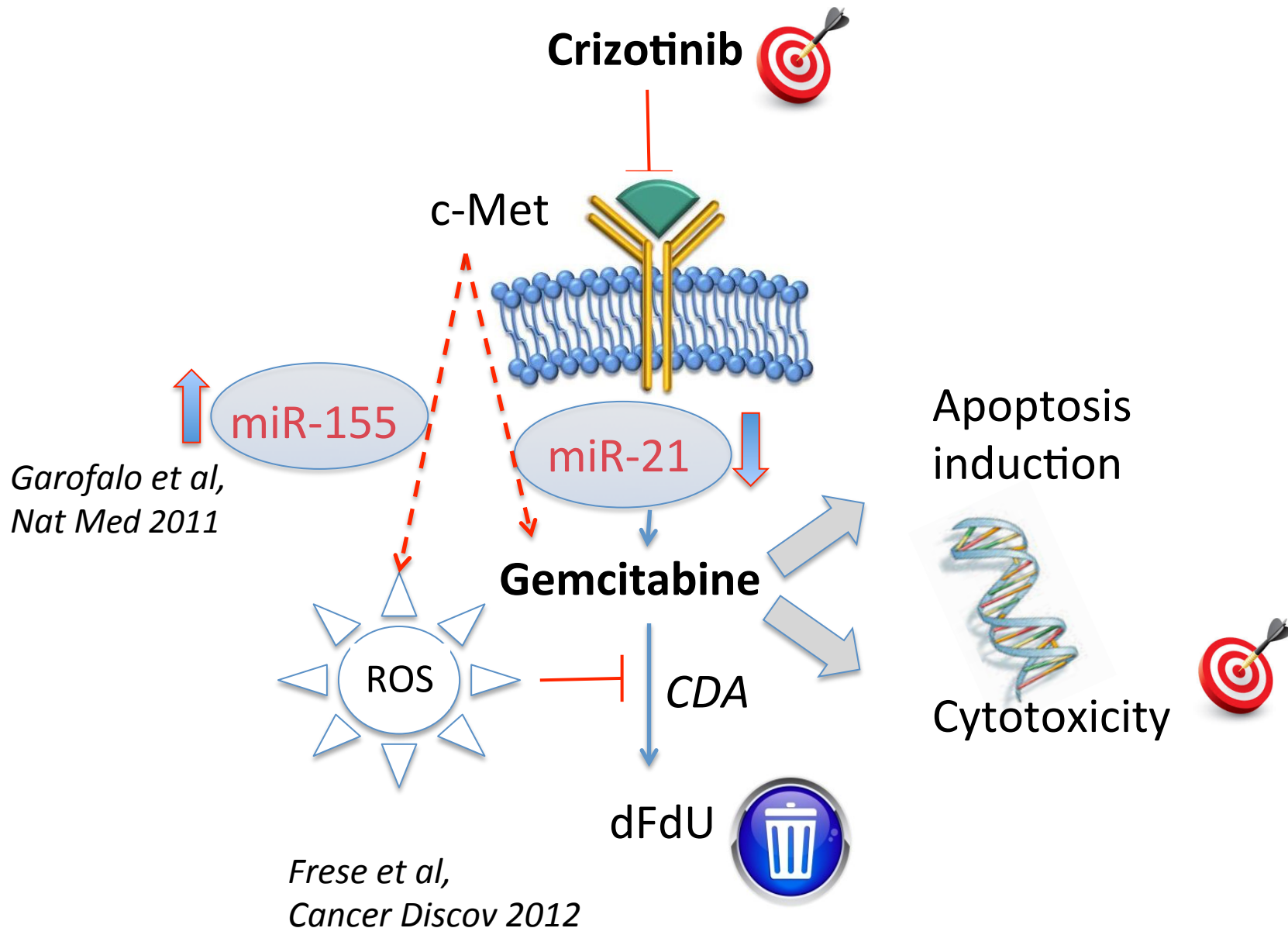
A proof-of-concept study,... and something more



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



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