UNIVERSITY OF MINNESOTA ROCHESTER

Emerin's Effect on Nuclear Dynamics Within Oncogenic KRAS-driven Pancreatic Cancer

Brian Chang

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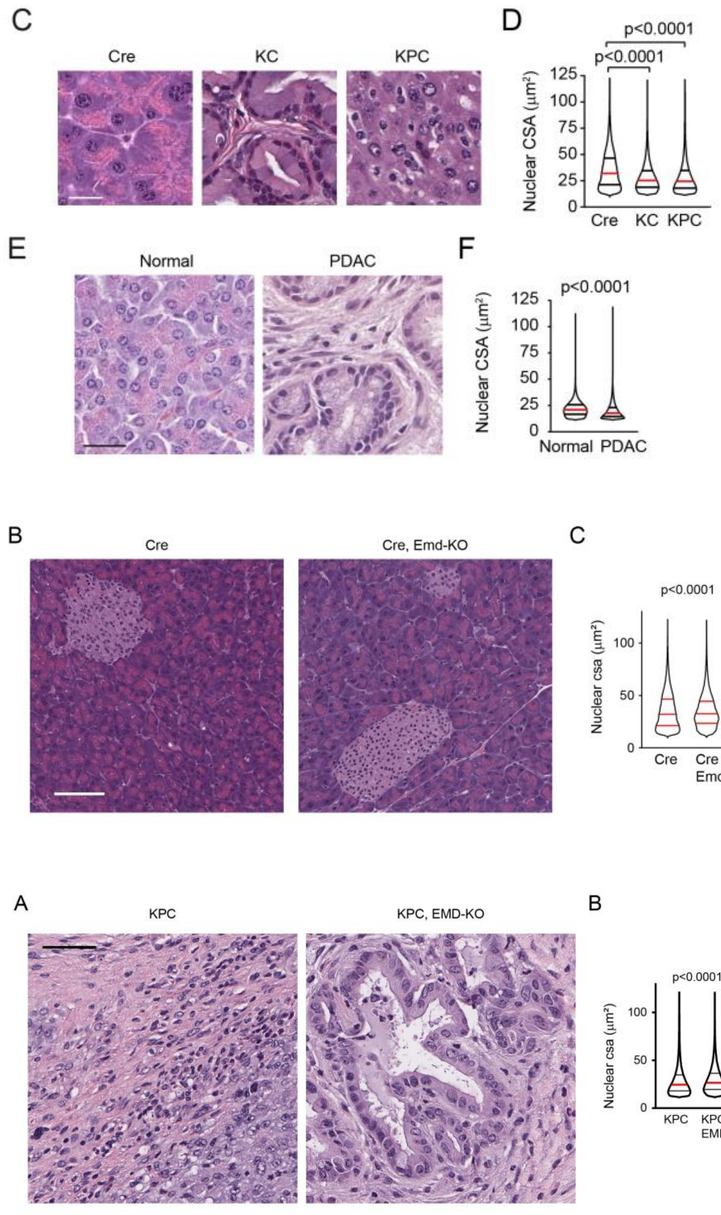
Abstract

Within diseased states and specifically pancreatic cancer, nuclear morphology is altered. There is not much information regarding the mechanism of action within different nuclear phenotypes, leading into unknown nature of the biological significance of nuclear size in carcinogenesis. Using both in vitro and in vivo models of pancreatic adenocarcinoma (PDAC), there was found to be an independent relationship regarding nuclear size reduction between cell proliferation and KRAS. KRAS gene mutations being common within pancreatic cancer proving its oncogenic nature. KRAS induced size reduction was a by product of the global reorganization of chromatin. Within PDAC cells, the nuclear lamina protein known as Emerin is known to alter the nuclear size through its relationship with Nesprin-3 by altering the keratin formation bordering the nucleus. In vivo testing of Emerin showed that it's absence within PDAC mouse models showed a decrease in high grade PDAC and an increase in nuclear size. Human analysis was also done to show this same relationship between PDAC grade and Emerin presence. This gives us more molecular information regarding size reduction in PDAC and its progression/state of carcinogenesis.

Introduction

- Utilizing the information known on the oncogenic nature of KRAS (present in over 90% of human PDAC cases), we wanted to figure out of if nuclear size alterations have a biological significance, within humans as well as mice utilizing doxycycline treatment which induces KRAS (+dox, -dox)

Methods



Conclusion

- Oncogenic KRAS expression decreases nuclear size in PDAC models, meaning that decreased nuclear size in human PDAC may be caused by KRAS signaling.
- It is hypothesized that emerin may influence the nuclear morphology by changing the arrangement of keratin intermediate filaments

Authors

Luis F. Flores 1 , David L. Marks 1 , Renzo E. Vera 1 , Ezequiel J. Tolosa 1 , Luciana L. Almada 1 , Kurt Berger 1 , Merih D. Toruner 1 , David R. Pease 1 , Brooke R. Tader 1 ,Katherine Wilson 2 , Christopher Pin 3 , Kyle Roux 4 , Martin E. Fernandez-Zapico 1 *. Add other authors?

Affiliations:
1 Schulze Center for Novel Therapeutics, Division of Oncology Research; Mayo Clinic, Rochester, MN, USA.
2 Department of Cell Biology, The Johns Hopkins University School of Medicine; Baltimore,
21205, Maryland, USA.
3 Departments of Pediatrics, Oncology, and Physiology and Pharmacology, Schulich School of
Medicine, University of Western Ontario Children's Health Research Institute; London, Ontario,
Canada.
4 Department of Pediatrics, Sanford School of Medicine, University of South Dakota; Sioux Falls,
SD, USA.