May 8th, 12:30 PM - 1:30 PM

Pregnancy Induces Persistent Changes that Potentiate Apoptotic Signaling and Responses to DNA Damage

Mary J. Hagen  
*University of Massachusetts Amherst*

Amy L. Roberts  
*University of Massachusetts Amherst*

Karen A. Dunphy  
*University of Massachusetts Amherst*

*See next page for additional authors*

Follow this and additional works at: [http://escholarship.umassmed.edu/cts_retreat](http://escholarship.umassmed.edu/cts_retreat)

Part of the [Cancer Biology Commons](http://escholarship.umassmed.edu/cts_retreat), [Translational Medical Research Commons](http://escholarship.umassmed.edu/cts_retreat), and the [Women's Health Commons](http://escholarship.umassmed.edu/cts_retreat)
Presenter Information
Mary J. Hagen, Amy L. Roberts, Karen A. Dunphy, Jeffrey L. Blanchard, Melissa A. Troester, Sallie S. Schneider, and D. Joseph Jerry

Creative Commons License
This work is licensed under a Creative Commons Attribution-Noncommercial-Share Alike 3.0 License.

This event is available at eScholarship@UMMS: http://escholarship.umassmed.edu/cts_retreat/2013/posters/50
Pregnancy Induces Persistent Changes that Potentiate Apoptotic Signaling and Responses to DNA Damage

Mary J. Hagen¹, Amy L. Roberts¹, Karen A. Dunphy¹,², Jeffrey L. Blanchard¹, Melissa A. Troester³, Sallie S. Schneider², D. Joseph Jerry¹,².
University of Massachusetts Amherst¹, Pioneer Valley Life Sciences Institute², University of North Carolina³

A full-term pregnancy reduces the lifetime risk of breast cancer by up to 50%. This effect is mediated, in part, by p53-dependent pathways. Gene expression profiling was used to investigate the mechanisms that alter apoptotic responses to DNA damage in the mammary gland. Radiation-induced responses in BALB/c-Trp53+/+ and BALB/c-Trp53-/- mice identified 121 genes that were altered by radiation and p53 status (p53-IR). To determine the effect of parity, mice were mated, force-weaned and mammary glands were allowed to involute for 21 days (parous) and compared with age-matched nulliparous mice. Gene expression profiles were determined in mammary tissues from nulliparous (N), parous (P), irradiated nulliparous (N-IR) and irradiated parous (P-IR) mice. The p53-IR gene signature did not differ among the N-IR and P-IR groups indicating that transcriptional activity of p53 was not altered by parity. However, expression profiles of apoptosis-related genes differed significantly in the parous group. The alterations in parous mammary tissues was accompanied by over-representation of biological processes that included “signal transduction” (e=1.69E-05). Within this set, Wnt signaling was especially pronounced (e<0.001). As TGFβ signaling has been implicated in multiple studies of parity-induced changes and Wnt5a was shown to be responsive to TGFβ, these genes were selected for epigenetic analysis. Primary mammary epithelial cells were isolated from N and P mice to determine patterns of active (H3K4me3) and repressed (H3K27me3) chromatin. Chromatin immunoprecipitation (ChIP) showed a 4-fold increase in the ratio of H3K4me3/H3K27me3 in parous mammary epithelium by qPCR. This was confirmed in preliminary ChIPseq experiments which identify global changes in chromatin.

Parity-regulated genes collaborate with p53-dependent targets, which act as a “switch”, to elicit apoptosis following ionizing radiation. The epigenetic states of the parity-regulated genes Tgfb2 and Wnt5a provide a mechanism for the persistent alterations in gene expression and apoptosis in parous mammary epithelial cells.

Grant support from NIEHS R01ES015739
Amy L. Roberts will be the presenting author