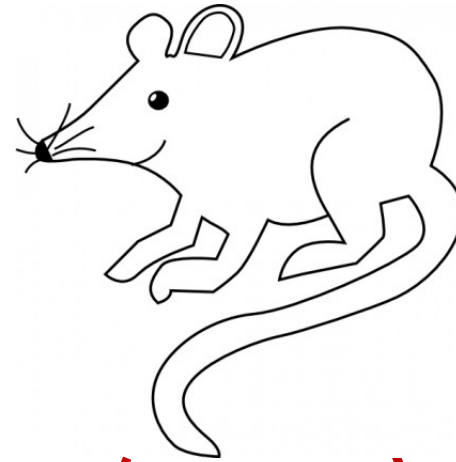
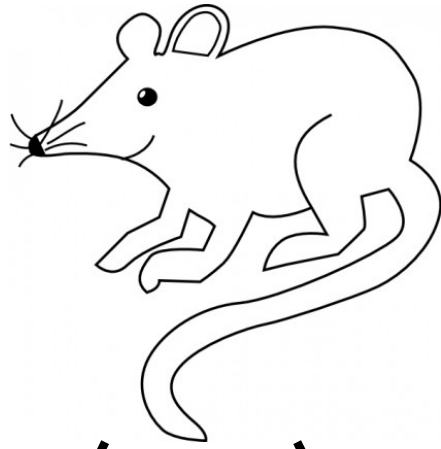


Alteration of mammary gland
development and gene expression
by *in utero* exposure to cadmium

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Georgetown University
Lombardi Comprehensive Cancer
Center

PREGNANT SPRAGUE-DAWLEY RATS

CONTROL



CADMIUM



control/control



control/cadmium



cadmium/control



cadmium/cadmium

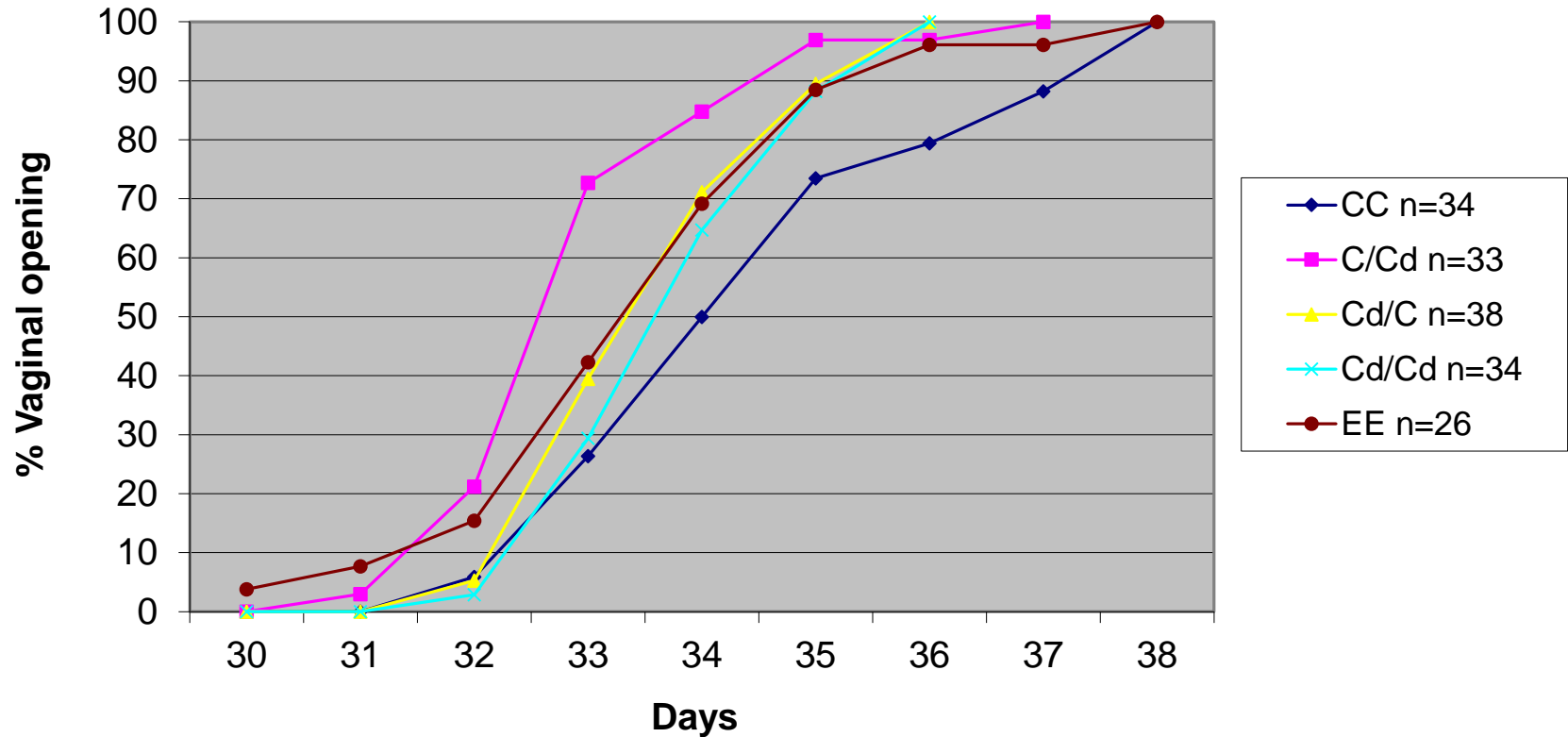
Mammary Gland

Structure and Cell Density

Stem/Progenitor Cells

Gene Expression

in utero and/or lactational effects of cadmium on vaginal opening



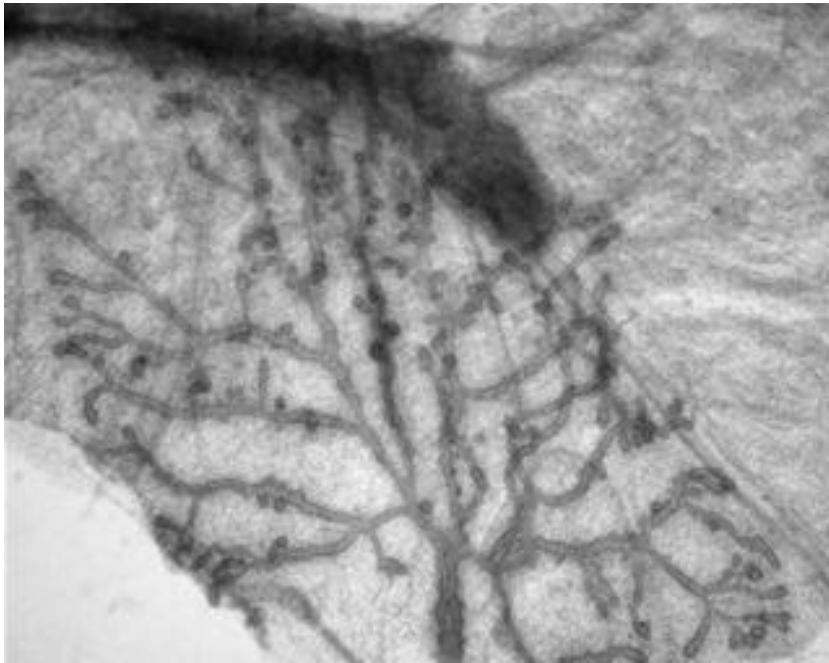
	CC	C/Cd	Cd/C	Cd/Cd	EE
Mean	34.76	33.24**	33.95*	34.15*	33.81*
SD	1.76	1.17	1.09	1.05	1.65
SE	0.3	0.2	0.18	0.18	0.32

* $p < 0.05$ when tested against CC

** $p < 0.0001$ when tested against CC

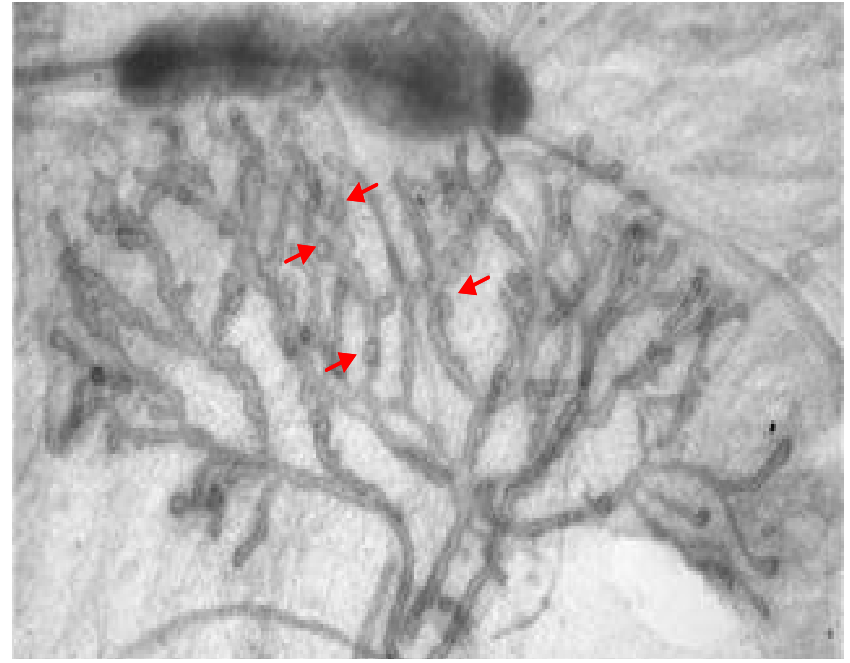
in utero effects of cadmium on mammary gland structure in female offspring (day 0)

A



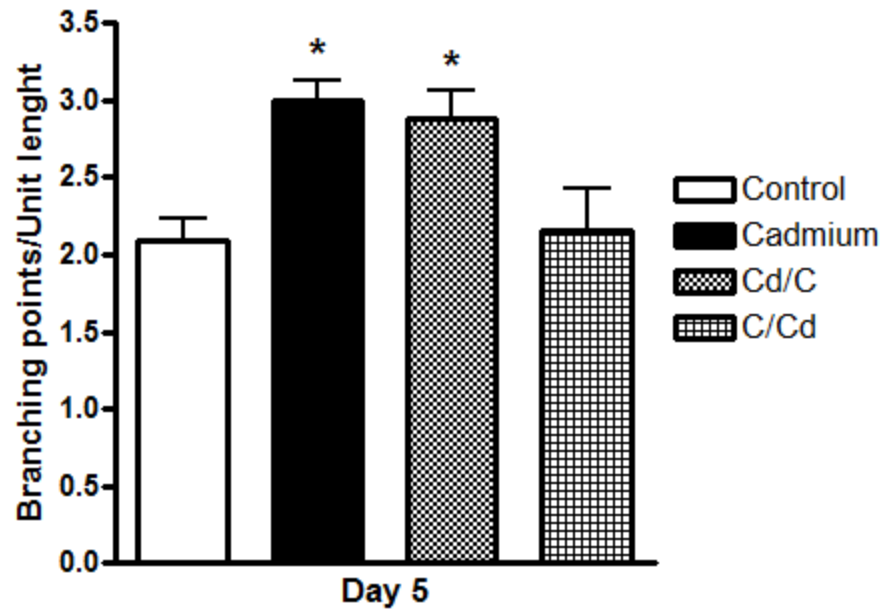
Control day 0

B



Cadmium day 0

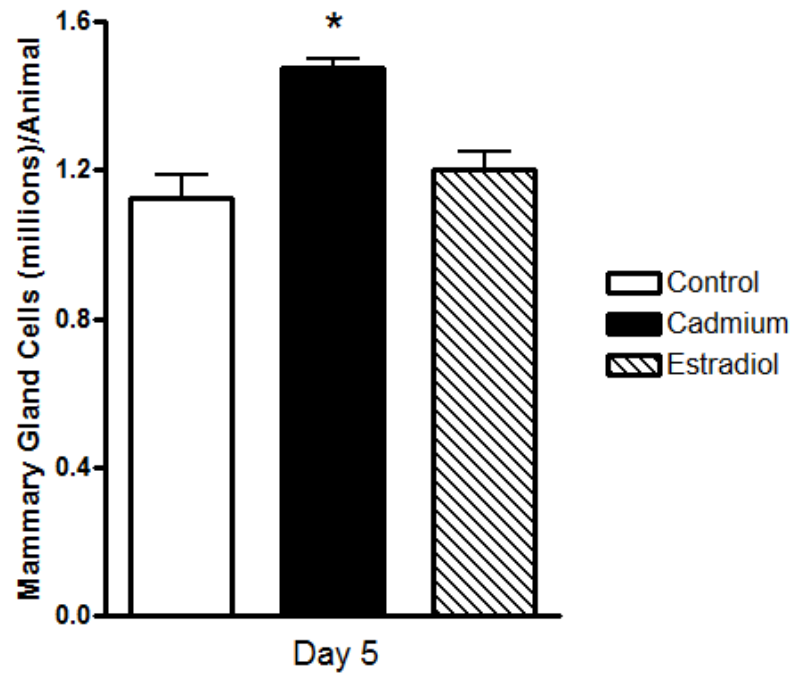
in utero effects of cadmium on mammary gland branching in female offspring (day 5)



n = 3

* p < 0.05 when tested against control

in utero effects of cadmium on mammary epithelial cells in female offspring (day 5)

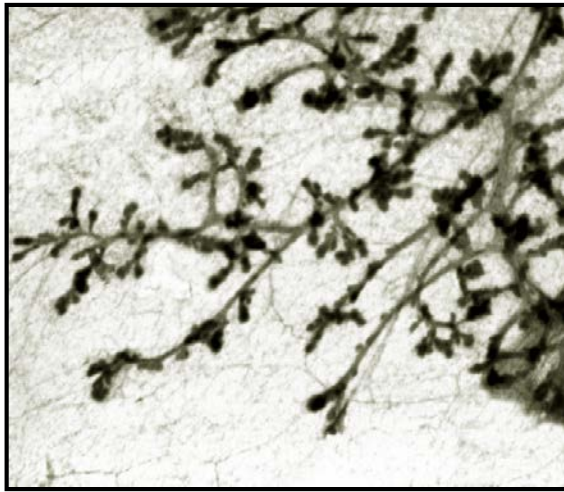


n = 3

* p<0.05 when tested against Control

in utero effects of cadmium on mammary gland density in female offspring

A

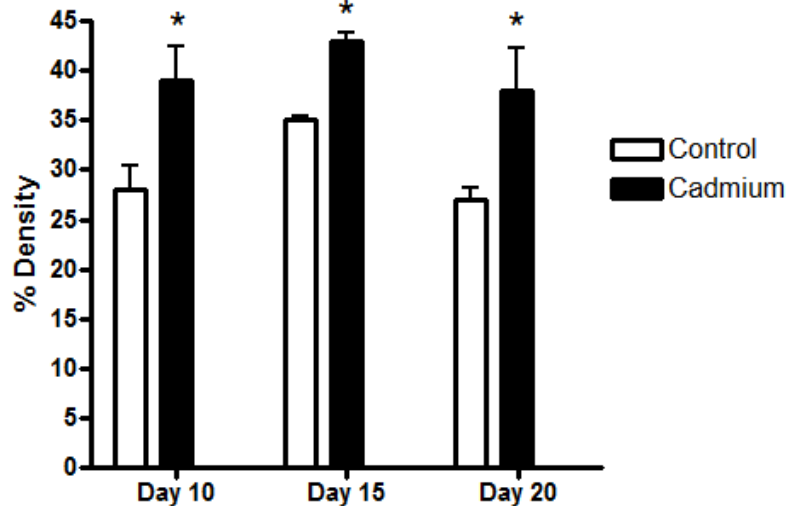


Control day15

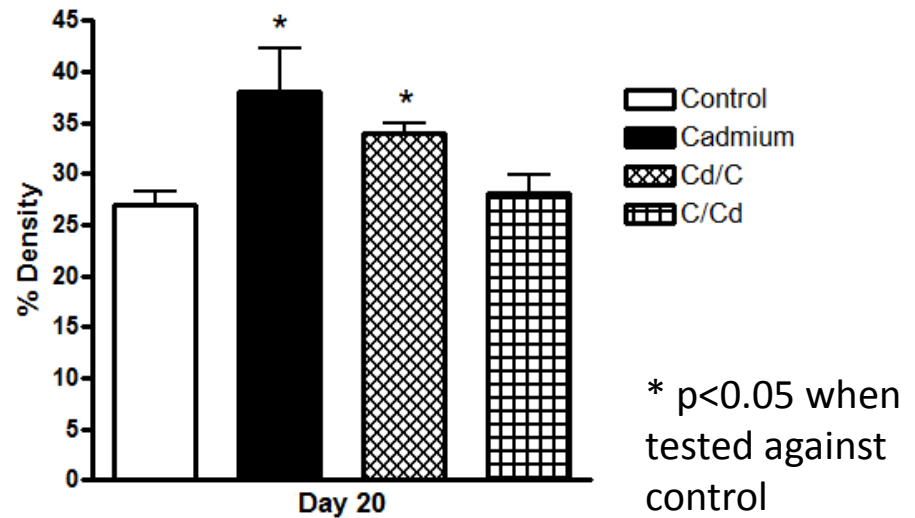


Cadmium day15

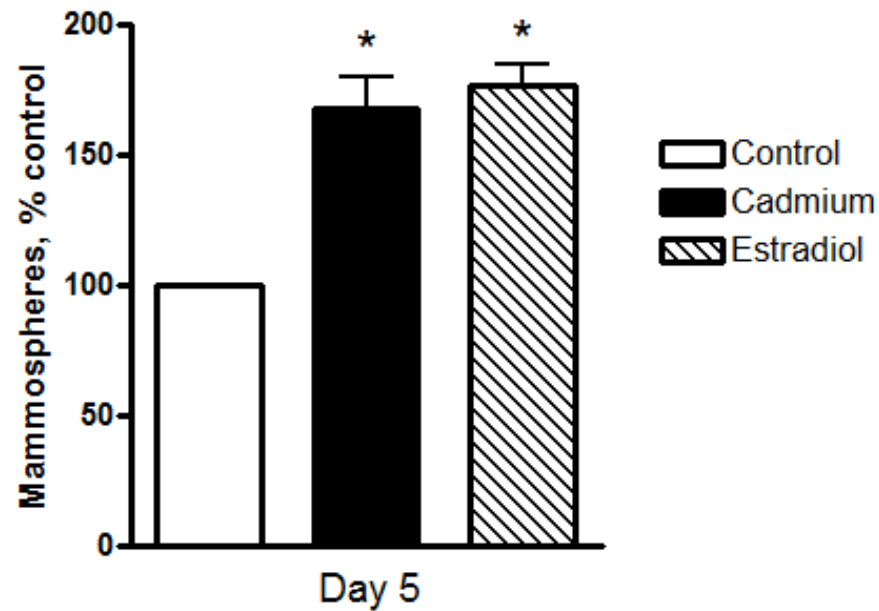
B



C



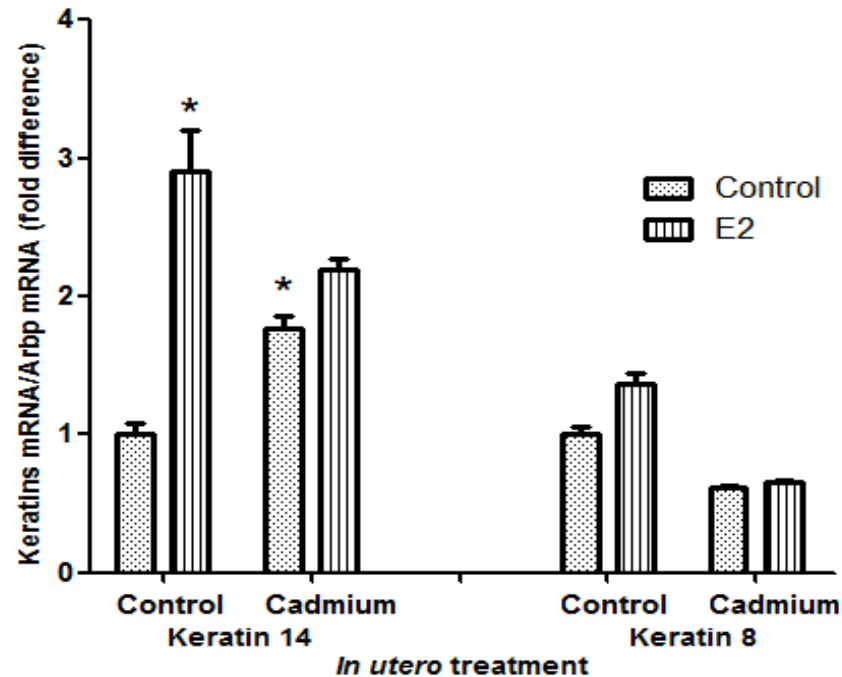
in utero effects of cadmium on number of mammospheres (day 5)



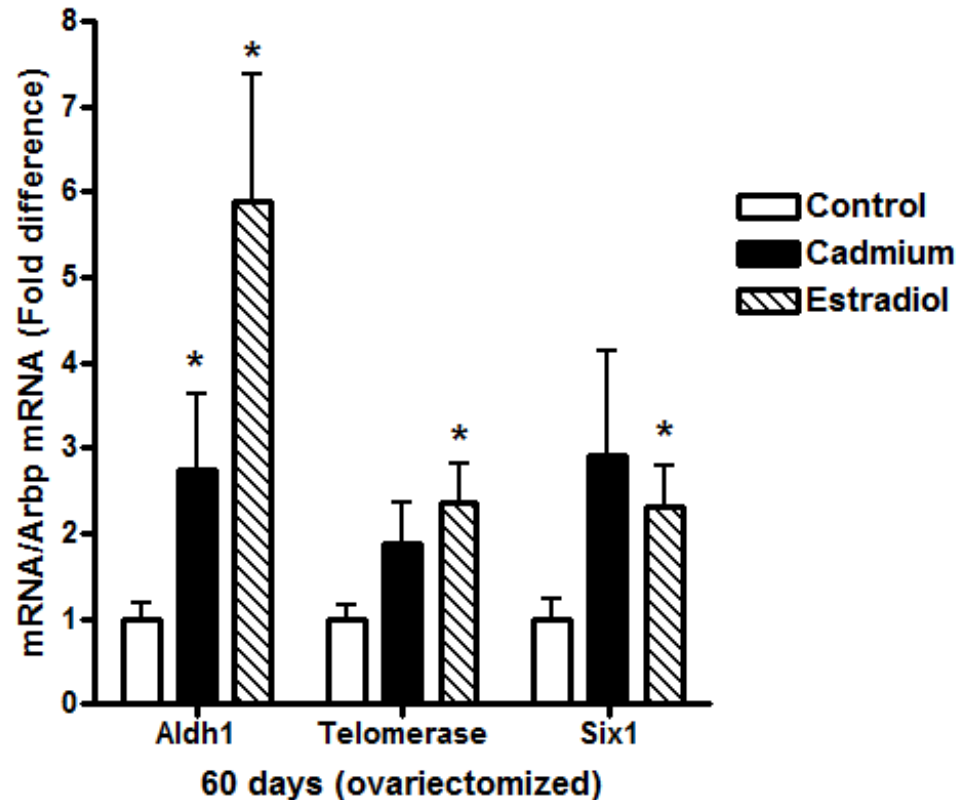
n = 3

* p<0.05 when tested against control

in utero effects of cadmium on mammary basal and luminal cell markers in female offspring (day 60; ovariectomized)



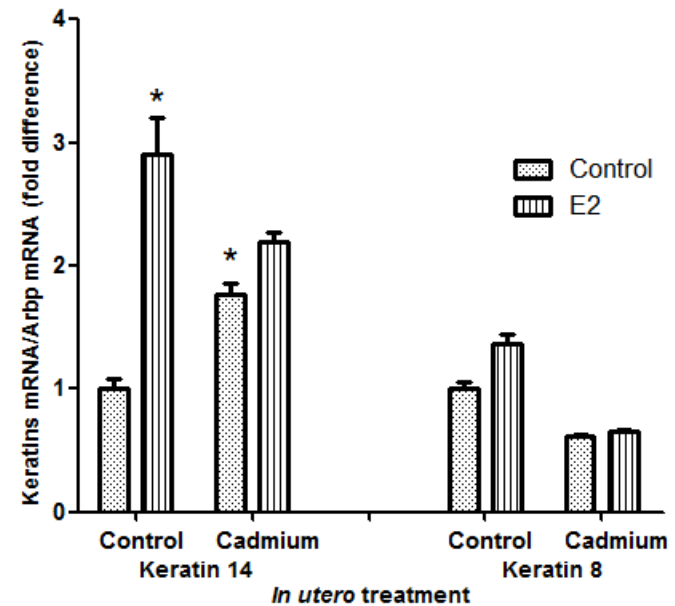
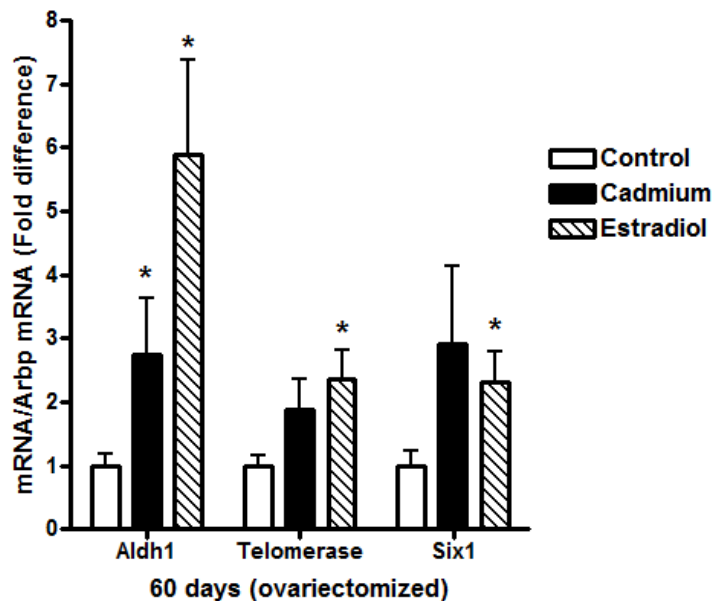
in utero effects of cadmium on mammary stem/progenitor cell markers in female offspring (day 60; ovariectomized)



n = 3 - 12

* p < 0.05 when tested against control

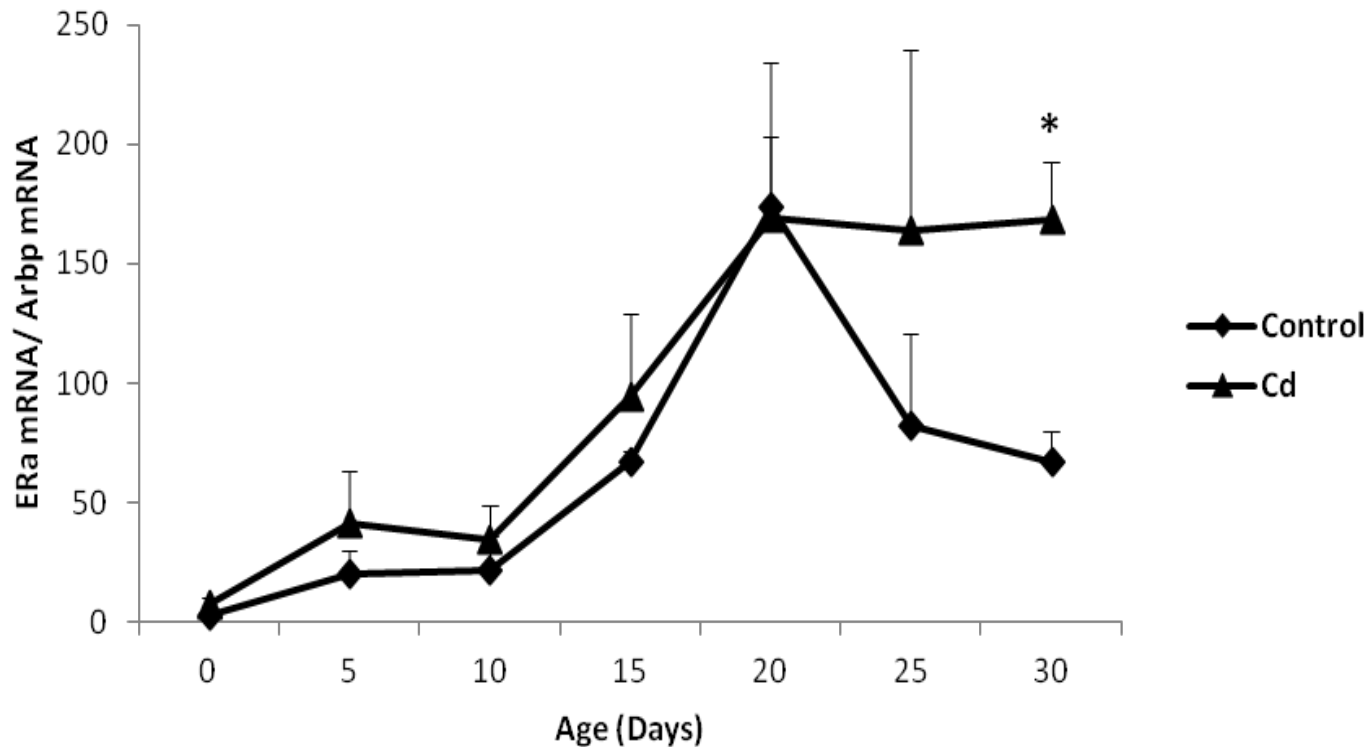
in utero effects of cadmium on mammary stem/progenitor cell markers in female offspring (day 60; ovariectomized)



n = 3 - 12

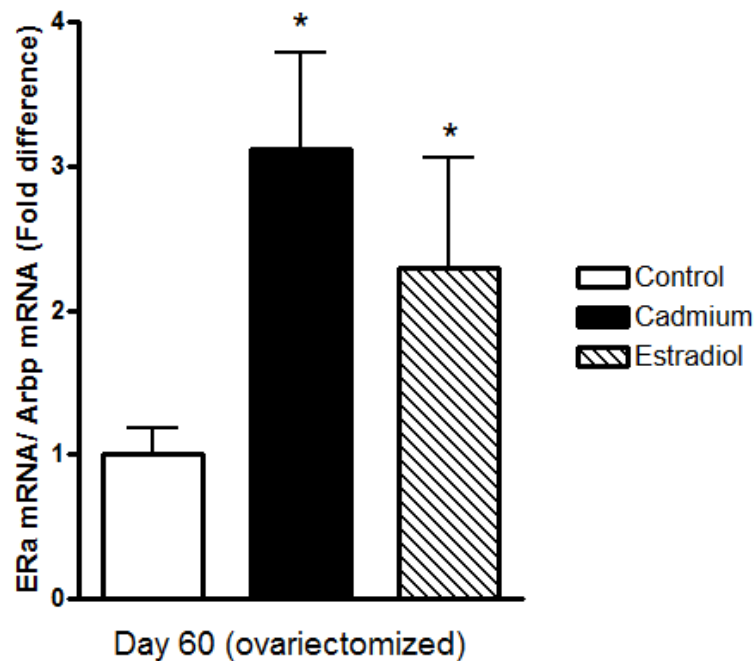
* p < 0.05 when tested against control

in utero effects of cadmium on ER α expression during development in mammary gland



* $p < 0.05$ when tested against control

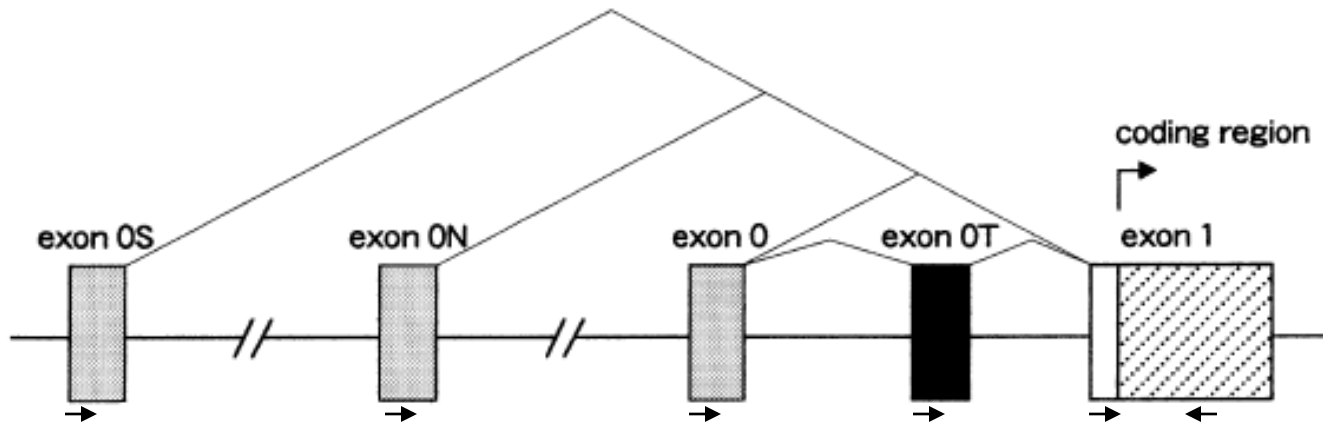
in utero effects of cadmium on mammary gland ER α expression in female offspring (day 60; ovariectomized)



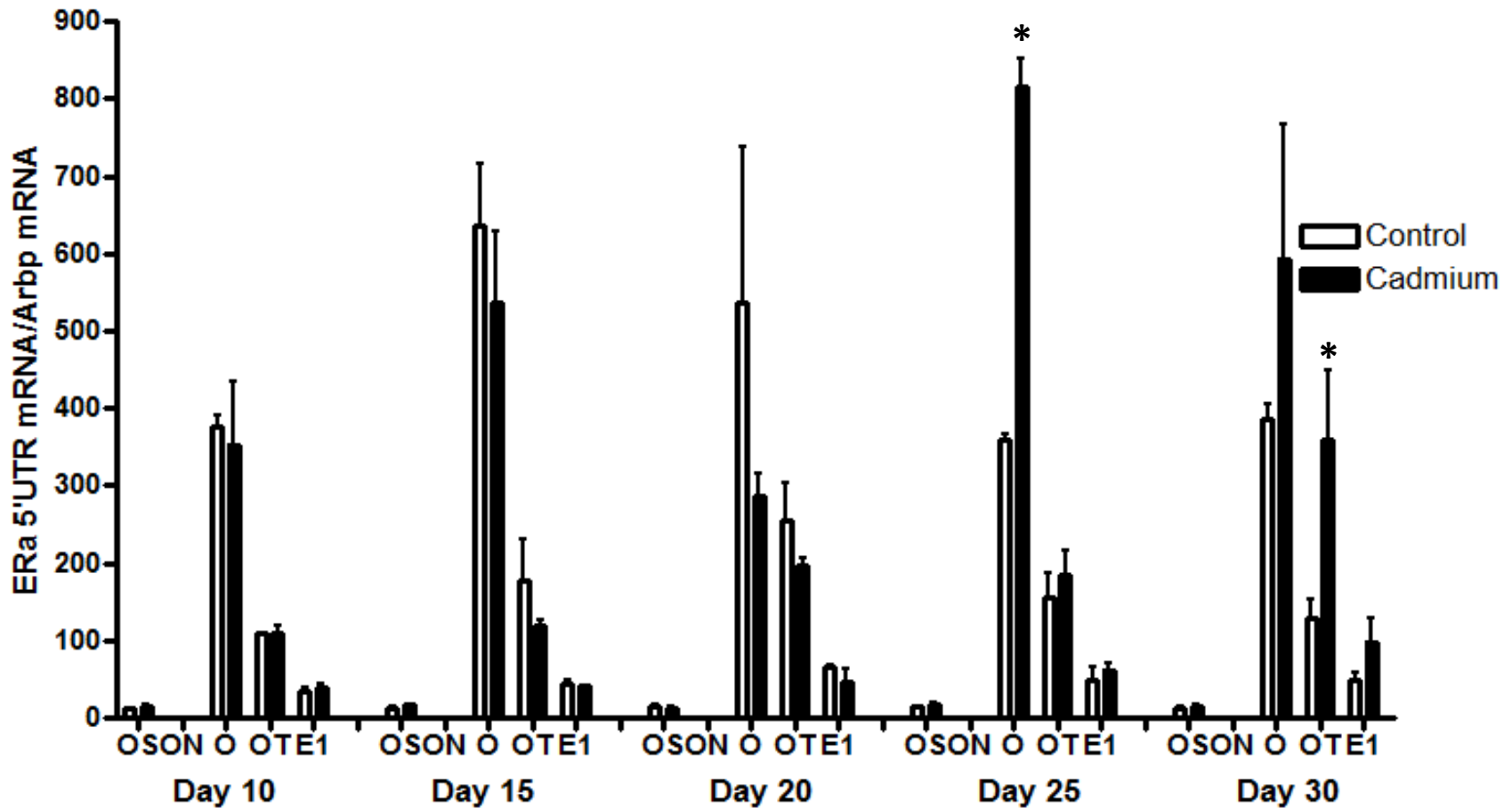
n = 3 - 12

* p<0.05 when tested against control

ER α promoter in rat



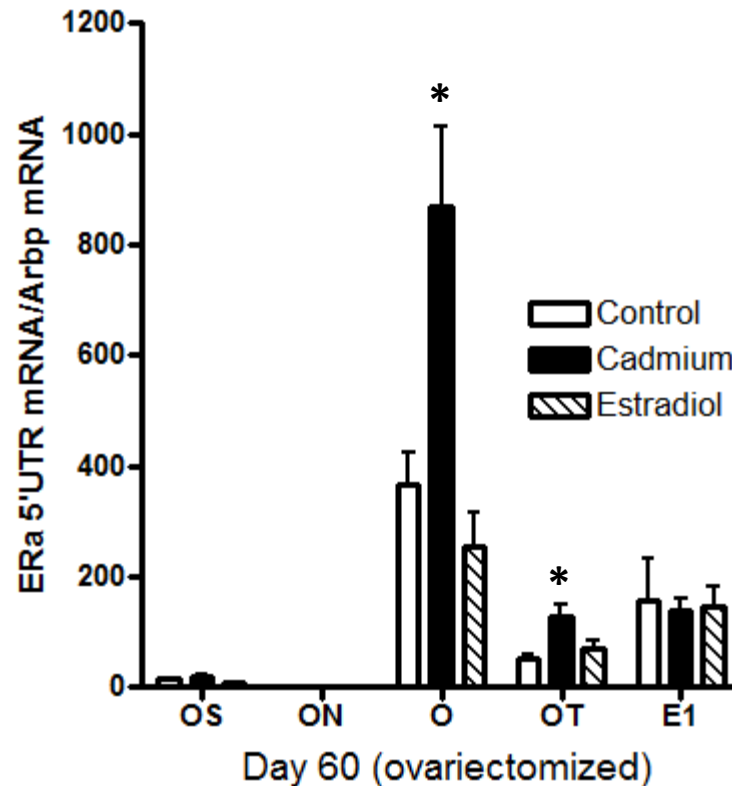
in utero effects of cadmium on expression of ER α 5'UTRs in female offspring (day 5-30)



n = 3

* p < 0.05 when tested against control

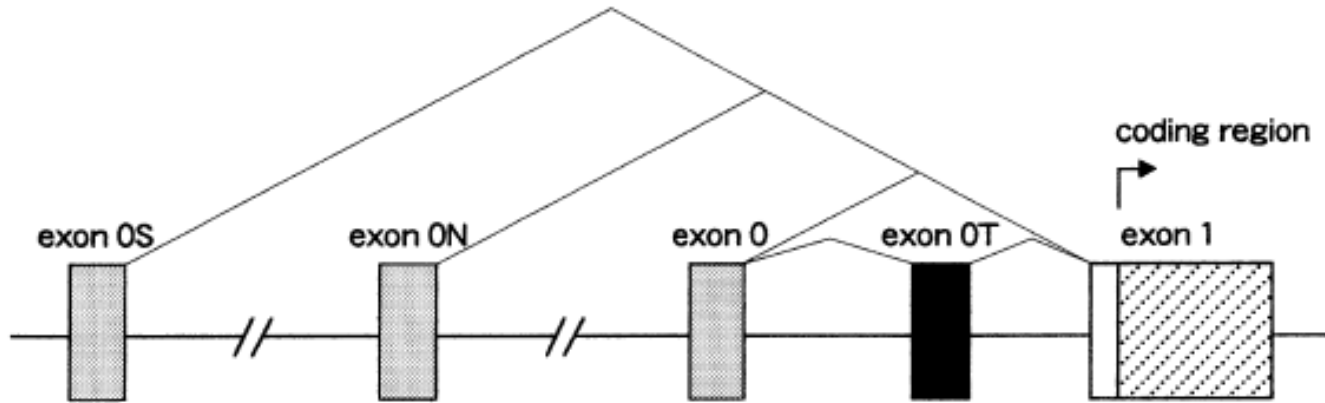
in utero effect of cadmium on the expression of ER α 5'UTR in female offspring (day 60; ovariectomized)



n = 3 - 12

* p < 0.05 when tested against control

ER α promoter in rat



in utero exposure rat



ER positive breast cancer



summary

- *in utero and lactational exposure to cadmium*
 - *accelerates puberty onset*
- *in utero exposure to cadmium*
 - *increases the number of stem/progenitor cells, branching, epithelial cells, and density*
 - *increases expression of ER α transcripts derived from exons O and OT*

does *in utero* exposure to cadmium increase the risk of developing breast cancer due to its ability to:

increase the number of mammary stem/progenitor (putative targets of malignant transformation)

increase the expression of ER α (thought to be the initial event in ER positive breast cancer)

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