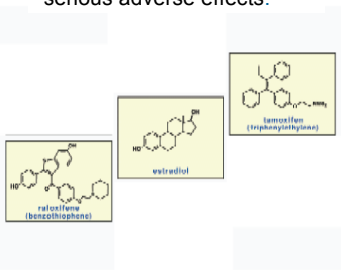
Elements by Selective Estrogen Receptor Modulators

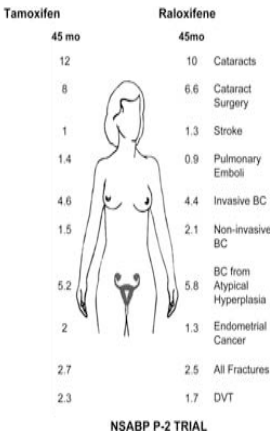
Lonnele J. Ball, Nitzan Levy, Gary L. Firestone and Dale C. Leitman,

Department of Obstetrics, Gynecology and Reproductive Sciences, Center for Reproductive Sciences, University of California, Berkeley, Department of Endocrinology and Molecular Cell Biology

Introduction

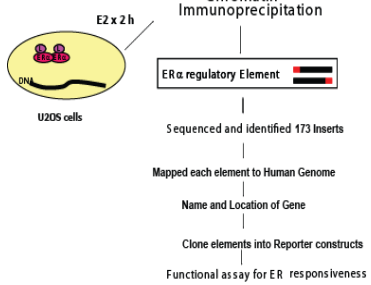
Tamoxifen and raloxifene are used to prevent breast cancer, but they cause serious adverse effects.

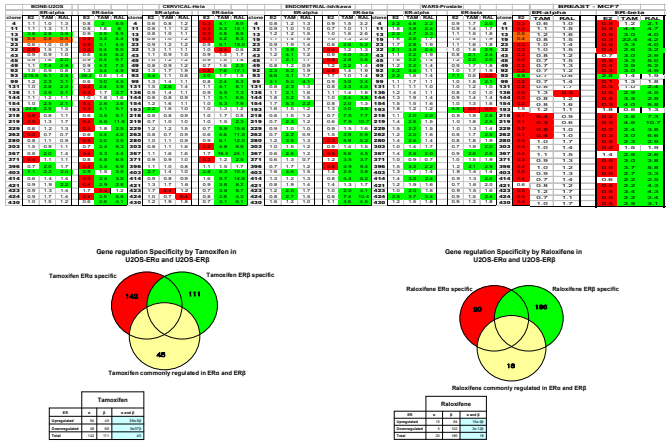


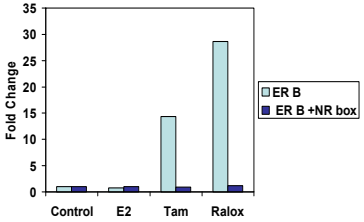


Goal

To determine molecular mechanisms causing the tissue specificity and different clinical effects of Selective Estrogen Receptor Modulators (SERMs)

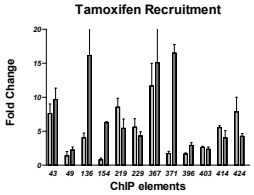


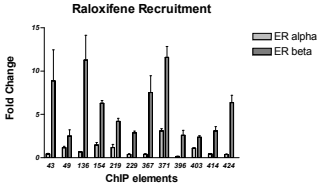


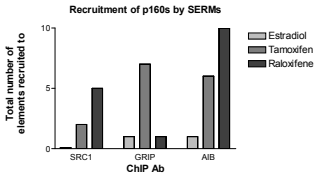


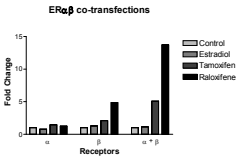
Summary of data with ChIP library in U2OS cells

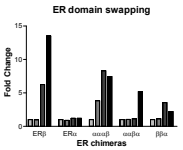
	Number of genes regulated by 2 fold or >
ERα	
Estradiol	18
Tamoxifen	47
Raloxifene	32
Tamoxifen > Raloxifene	28
Raloxifene > Tamoxifen	5
ERβ	
Estradiol	15
Tamoxifen	30
Raloxifene	117
Tamoxifen > Raloxifene	3
Raloxifene > Tamoxifen	111

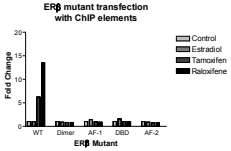












Conclusion:

- The ChIP library isolated authentic ER regulatory elements that are SERM-specific regulatory elements (SERM-RE), activated by the SERMs, but not estradiol
- SERM-specific regulatory elements and endogenous genes are regulated in a tissue specific and ER subtype selective manner by SERMs
- Transcriptional activation by SERMs is mediated by distinct patterns of co-activator recruitment and possibly by other coregulatory proteins and transcription factors

Acknowledgements

A special thank you to Isaac Cohen and members of the Leitman Lab including Dale Leitman, Tatjana Zogovic, Nitzan Levy and UCB Endocrinology Department