Genome-wide coexpression of steroid receptors in the mouse brain: identifying signaling pathways and functionally coordinated regions

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Genome-wide co-expression of steroid receptors in the mouse brain: identifying signaling pathways and

Introduction

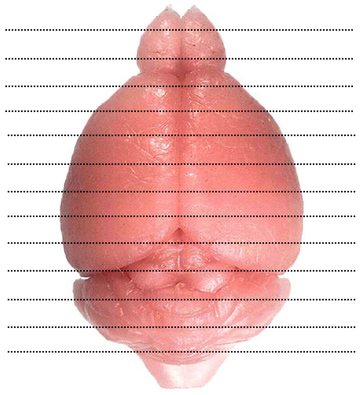
Steroid hormones coordinate the activity of many brain regions by binding to nuclear receptors that act as transcription factors. This study uses genome wide correlation of gene expression in the mouse brain to:

1) find brain regions that respond in a similar manner to particular steroids,
2) identify signaling pathways that are used in a steroid receptor and brain region-specific manner, and
3) discover potential target genes and relationships between groups of target genes.

The data constitute a rich repository for the research community to support further new insights in neuroendocrine relationships, and to develop novel ways to manipulate brain activity in research or clinical settings.

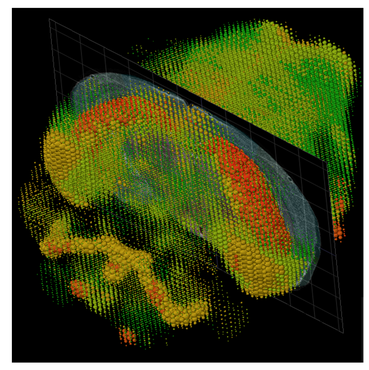
Allen Brain Atlas[1]

Mouse Brain

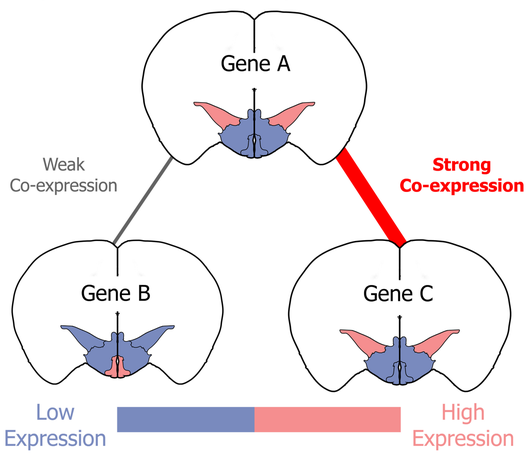


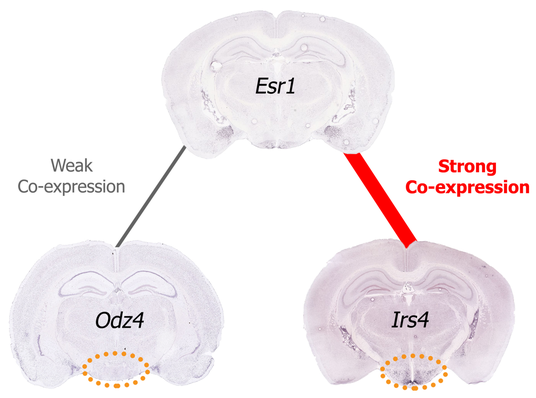
~22,000 Genes

3D Expression Map

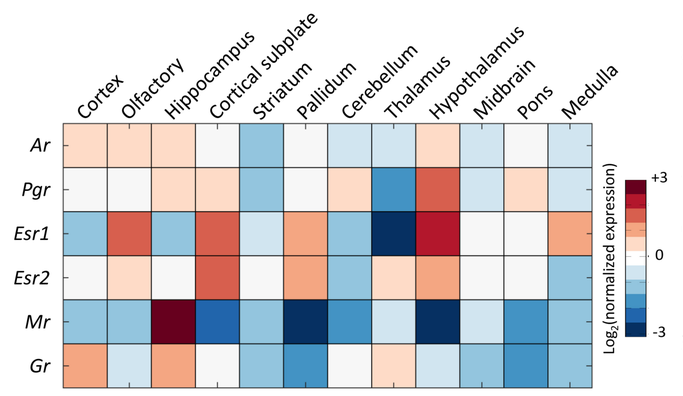


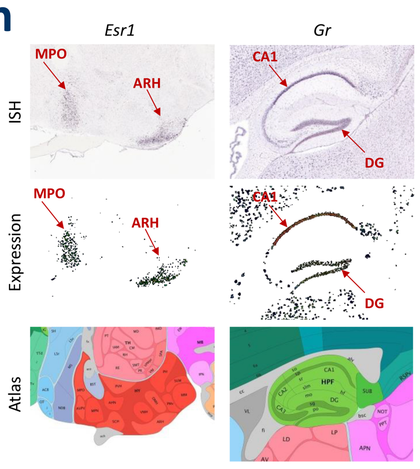
Spatial Co-expression





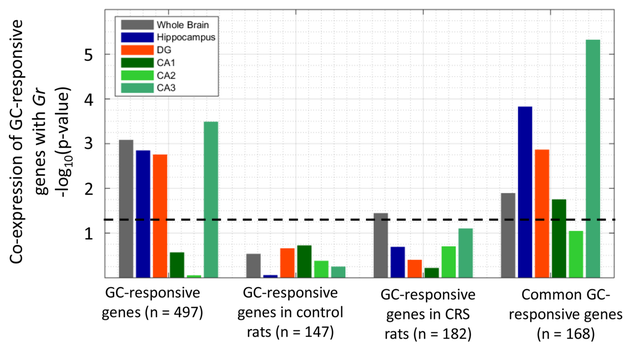
Receptors Expresion in the Brain

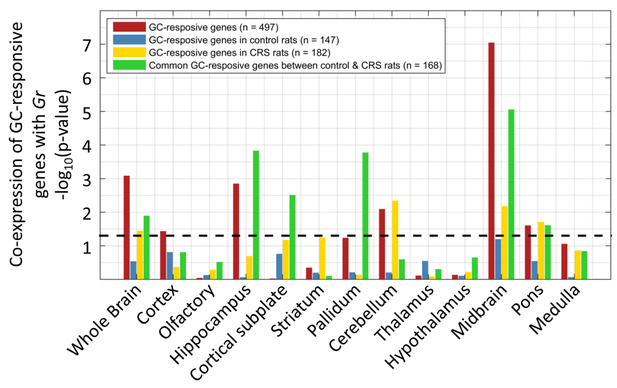




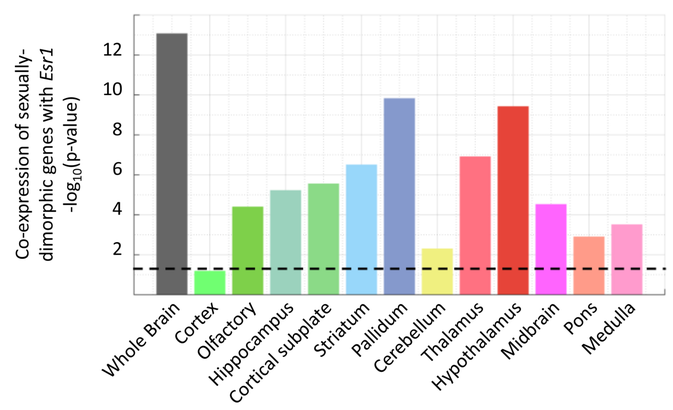
Co-expression of Target Genes

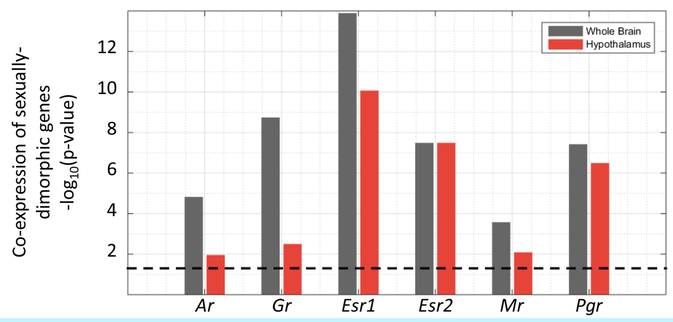
Glucocorticoid-responsive genes[2] and *Gr*



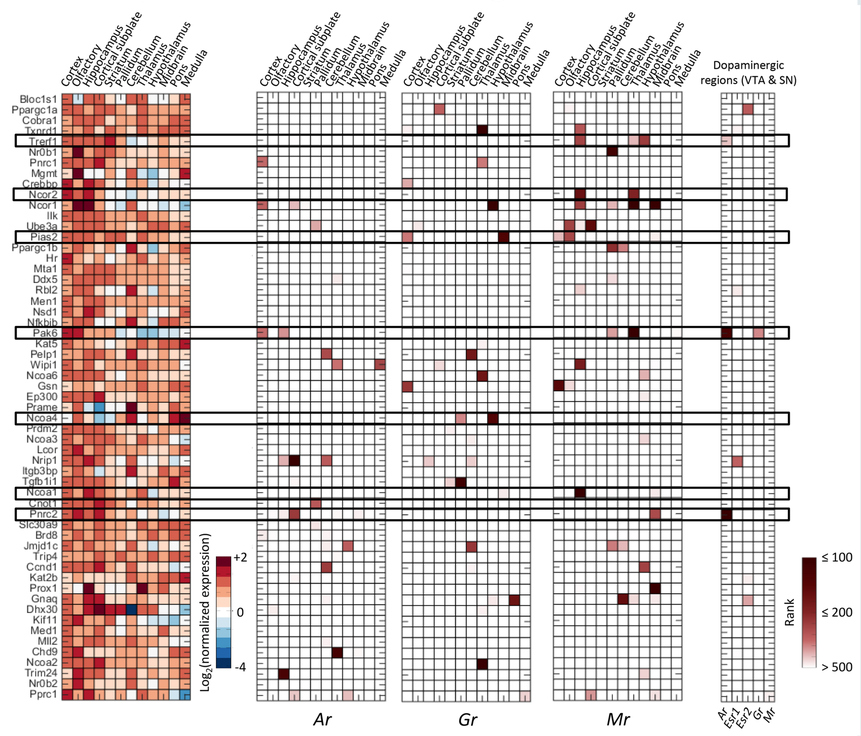


Sexually-dumorphic genes[3] in the hypothalaums and *Esr1*





Co-expression of Co-regulators[4]



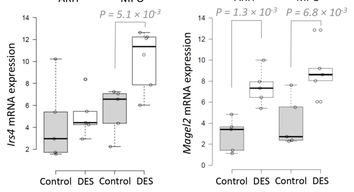
Pak6 likely mediates Ar effects on dopaminergic transmission in the Ventral Tegmental Area (VTA) and Substantia Nigra (SN)

Using Co-expression to Predict Hormone Responsiveness

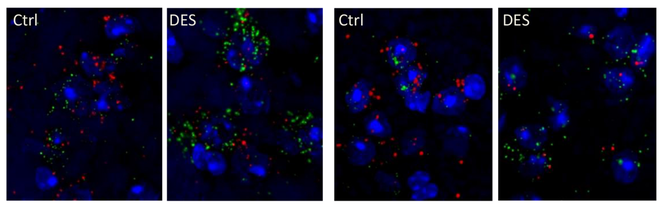
Response of *Ers1*-co-expressed genes to estrogen diethylstilbesterol (DES) treatment in the hypothalamus (qPCR)

	Gene	Correlation	Correlation Rank	Expression*	Expression Rank	Anterior HY (fold change)	Anterior HY (p-value)	Posterior HY (fold change)	Posterior HY (p-value)
*	**Irs4**	0.79	1	7.24	1	**1.45**	0.04	**1.26**	0.19
	Fut8	0.75	2	0.36	3367	1.10	0.32	1.34	0.23
	Gdpd2	0.66	4	3.54	42	**1.34**	0.04	**1.08**	0.24
	Ngb	0.64	6	6.24	8	**1.44**	0.05	**1.24**	0.21
	Rfx7	0.63	7	0.98	1195	1.16	0.24	1.08	0.14
	Adck4	0.62	8	1.98	141	**1.31**	0.05	**1.30**	0.09
	Ltbp4	0.60	9	1.13	737	1.20	0.12	0.87	0.14
*	**Magel2**	0.57	11	5.63	11	**1.47**	0.06	**1.25**	0.18
	Unc5d	0.57	13	1.52	284	**1.32**	0.10	**1.34**	0.08
	Bhlhb9	0.57	15	0.62	2473	1.17	0.11	1.02	0.39

Double in situ hybridization of *Irs4* and *Magel2* with *Esr1* in the hypothalamus



Response of *Irs4* to DES treatment in castrated mice



Response of *Magel2* to DES treatment in castrated mice

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