

Age-Associated Endocrine Dysfunction Increases Risk of Neurodegenerative Diseases

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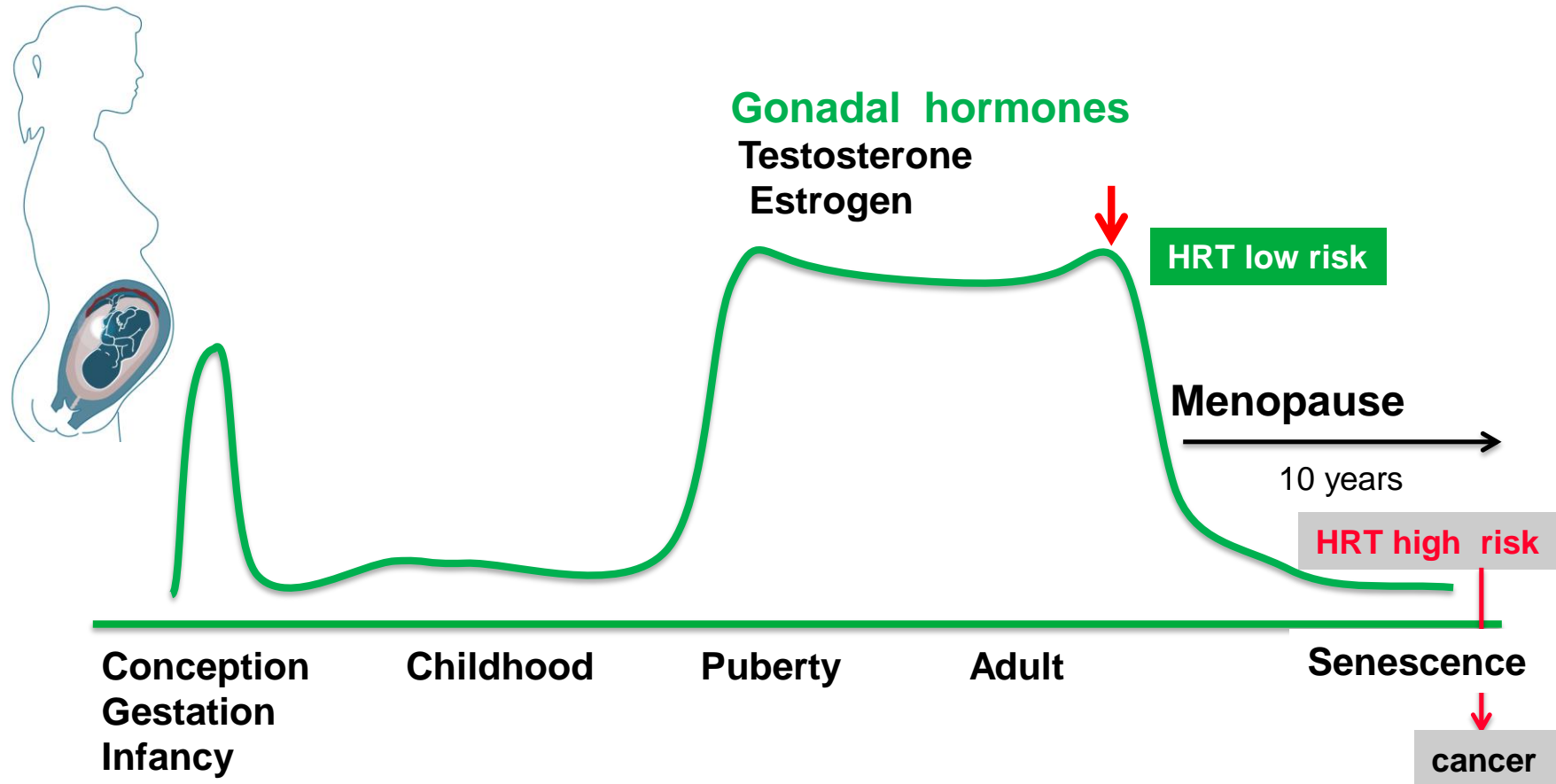
MEIJI UNIVERSITY MAY19-25, 2019



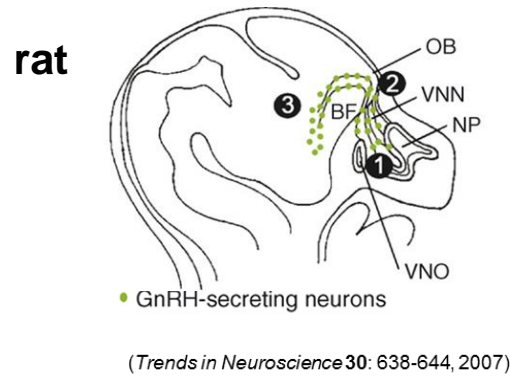
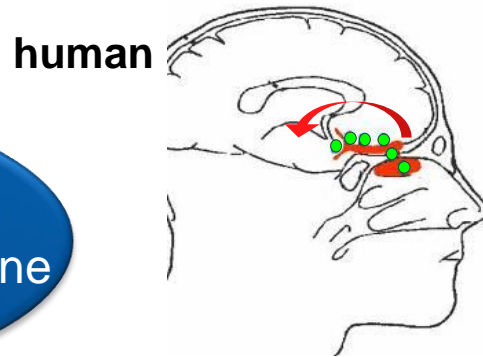
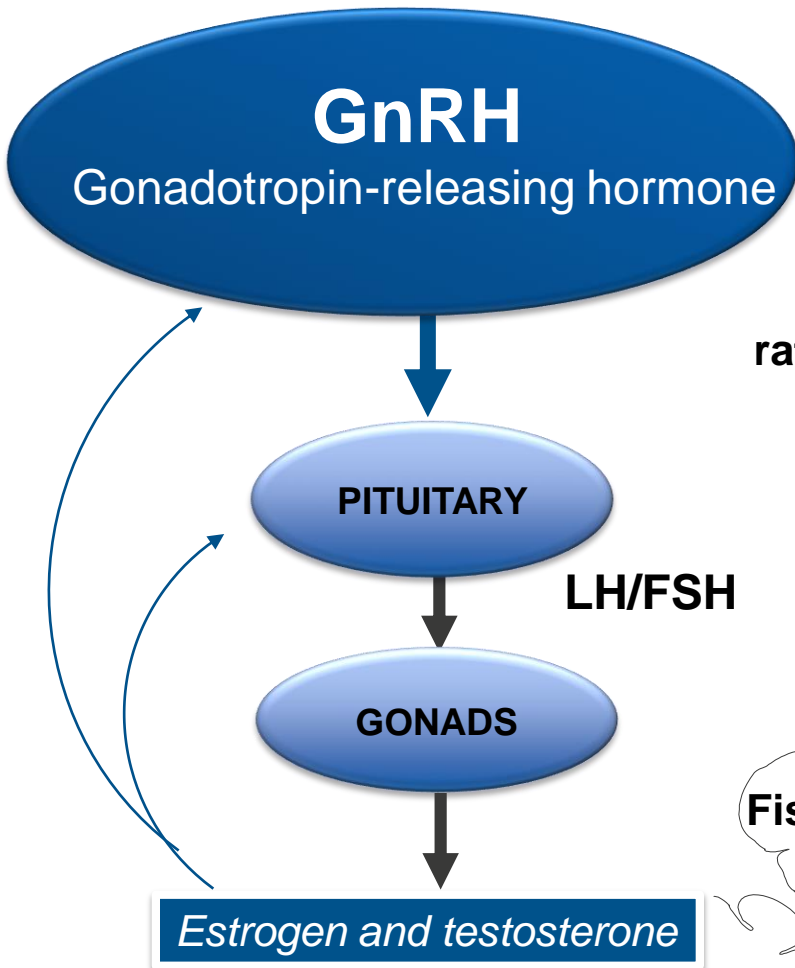
Sex Differences in Neurodegenerative and Neuropsychiatric Diseases

Disease	Women : Men (%)
Rett syndrome	100 : 0
Anorexia nervosa	93 : 7
Bulimia	75 : 25
Alzheimer's Disease	74 : 26
Posttraumatic stress disorders	70 : 30
Anxiety disorder	67 : 33
Depression	63 : 37
Parkinson's Disease	40 : 60
Amyotrophic lateral sclerosis	33 : 67
Schizophrenia	27 : 73
ADHD	20 : 80
Autism	20 : 80
Kallmann's syndrome	17 : 83
Kleine-Levin syndrome	0 : 100

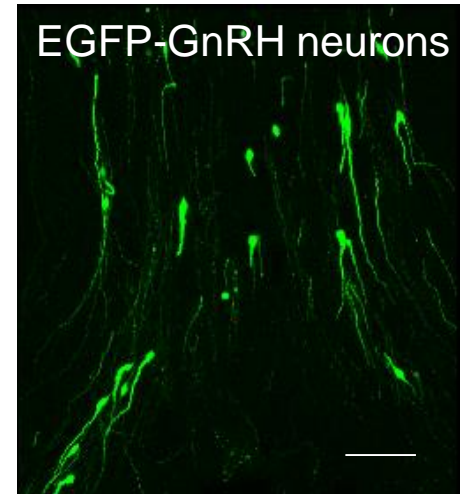
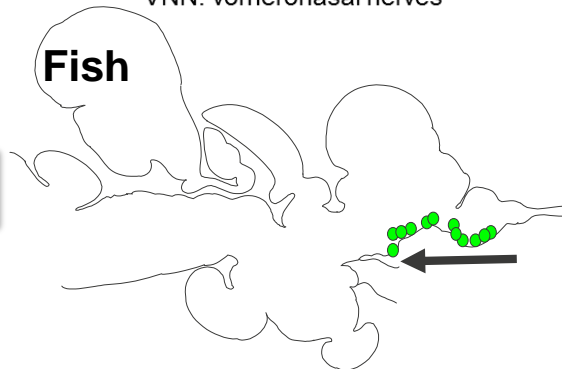
THERAPEUTIC USE OF STEROIDS



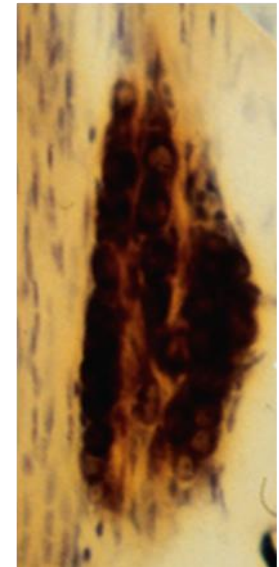
Hypothalamic Regulation of Reproduction



VNO : the vomeronasal organ
VNN: vomeronasal nerves



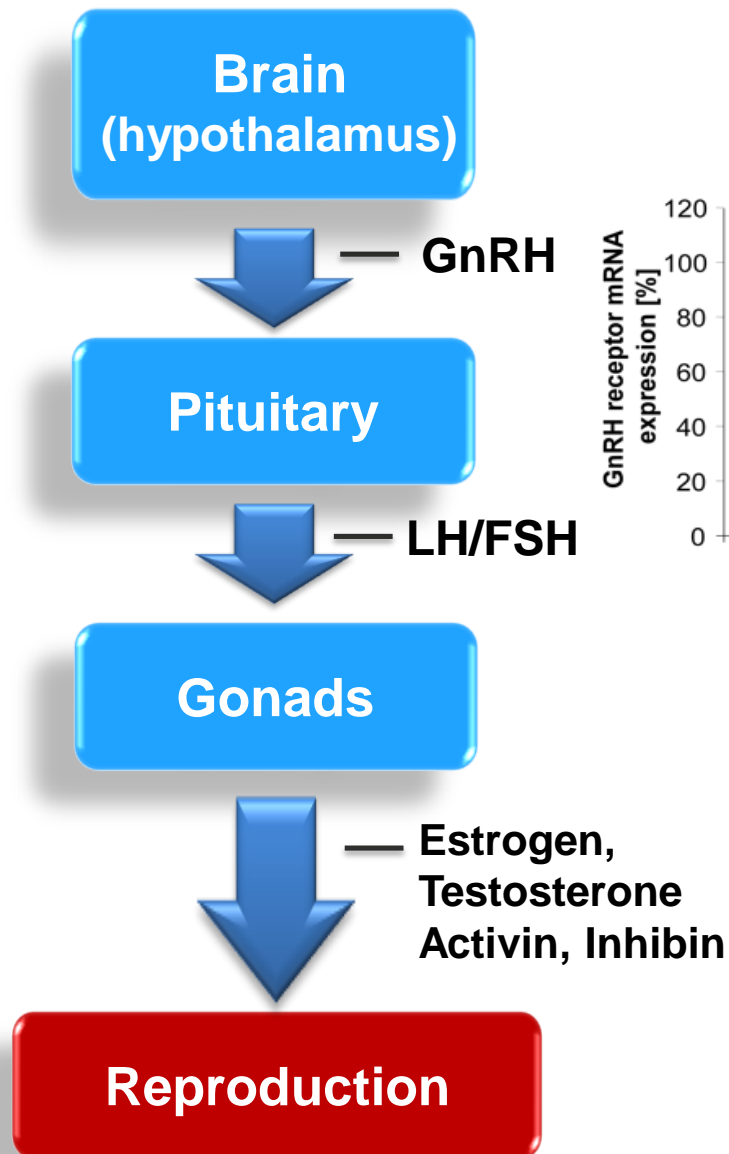
SALMON



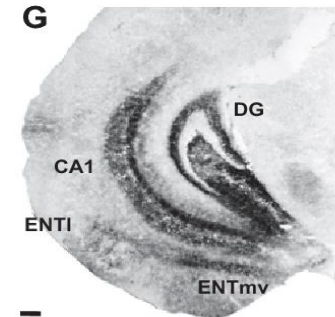
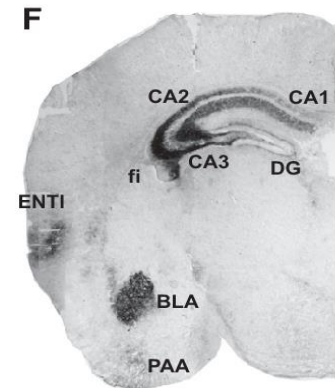
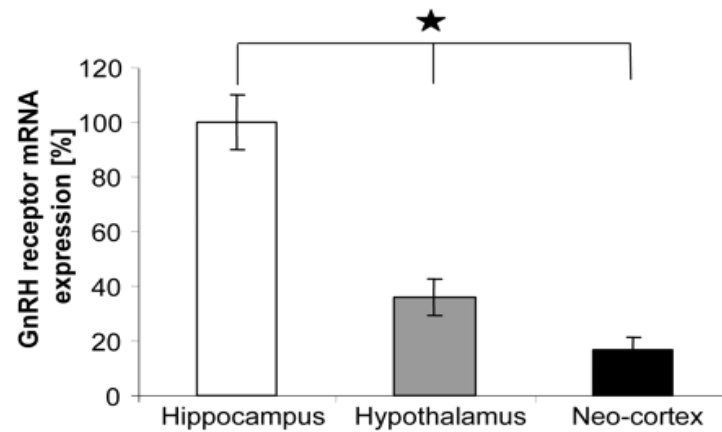
Evolutionarily conserved

Parhar et al (1993) *Neurosci lett*
Lim, Parhar et al (2013) *Cell and Tissue Research*

HYPOTHALAMUS

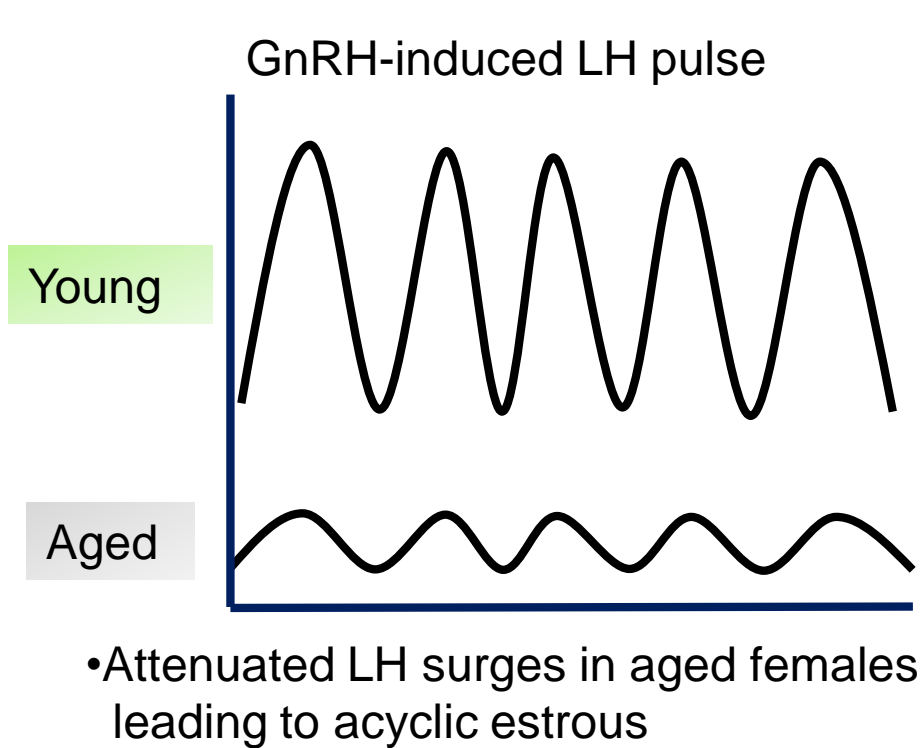


GnRH-R in hippocampus



cognition

Central reproductive peptide



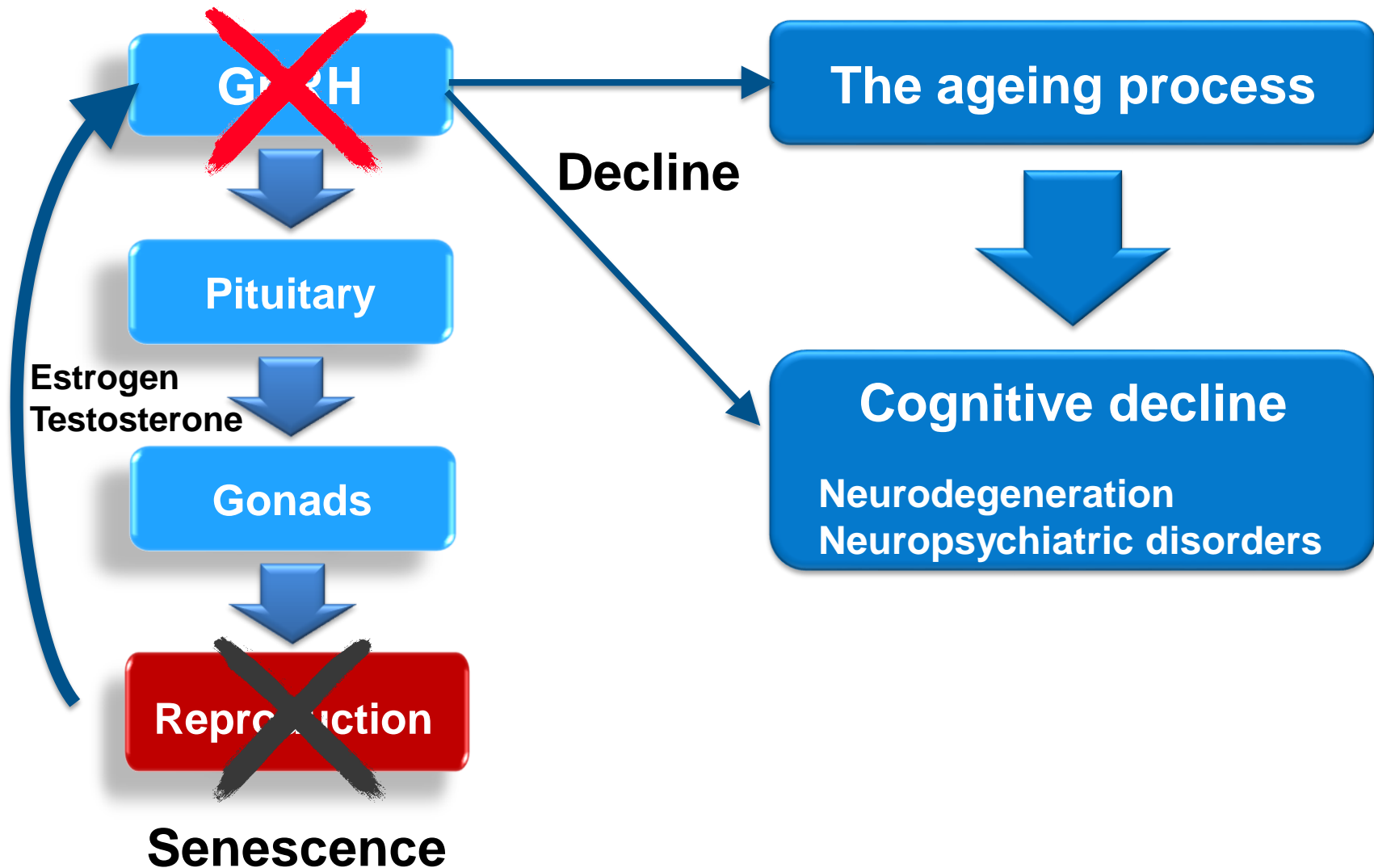
Aged GnRH neuronal characteristics

- Unaltered neuronal numbers, morphology and distribution
- Altered GnRH terminals
- Decreased GnRH pulsatile release
- Decreased GnRH neuronal activation

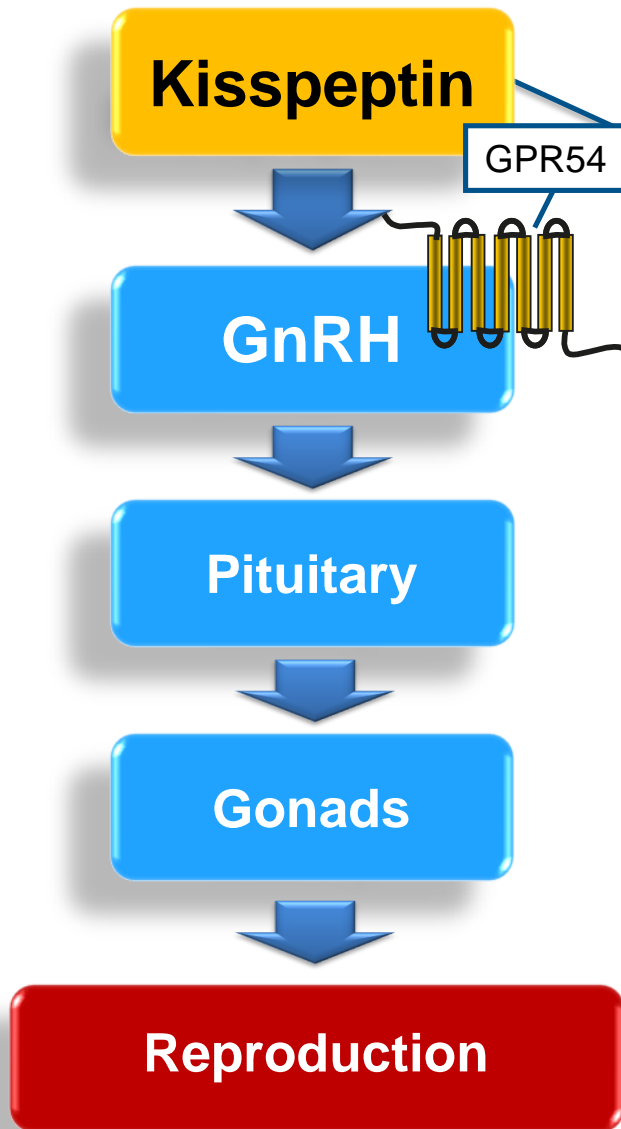


Neurodegenerative Disease

The Reproductive Axis

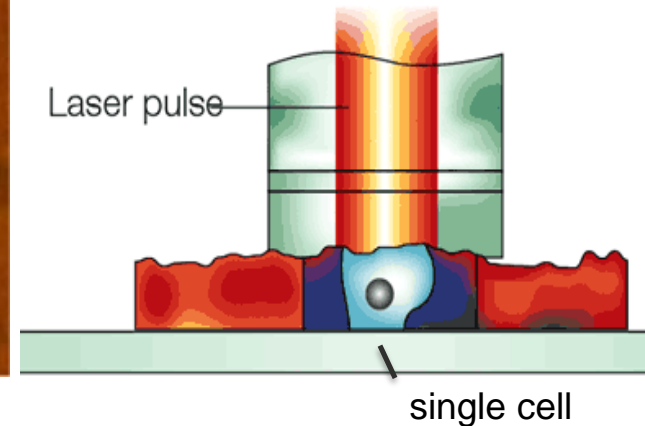
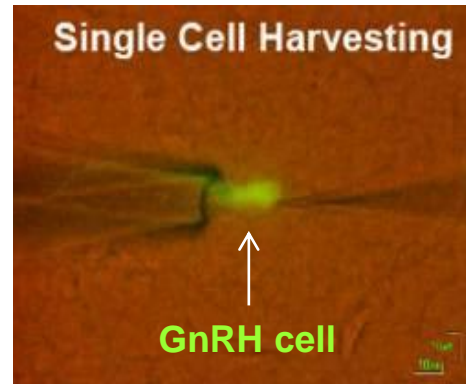


Reproductive Axis

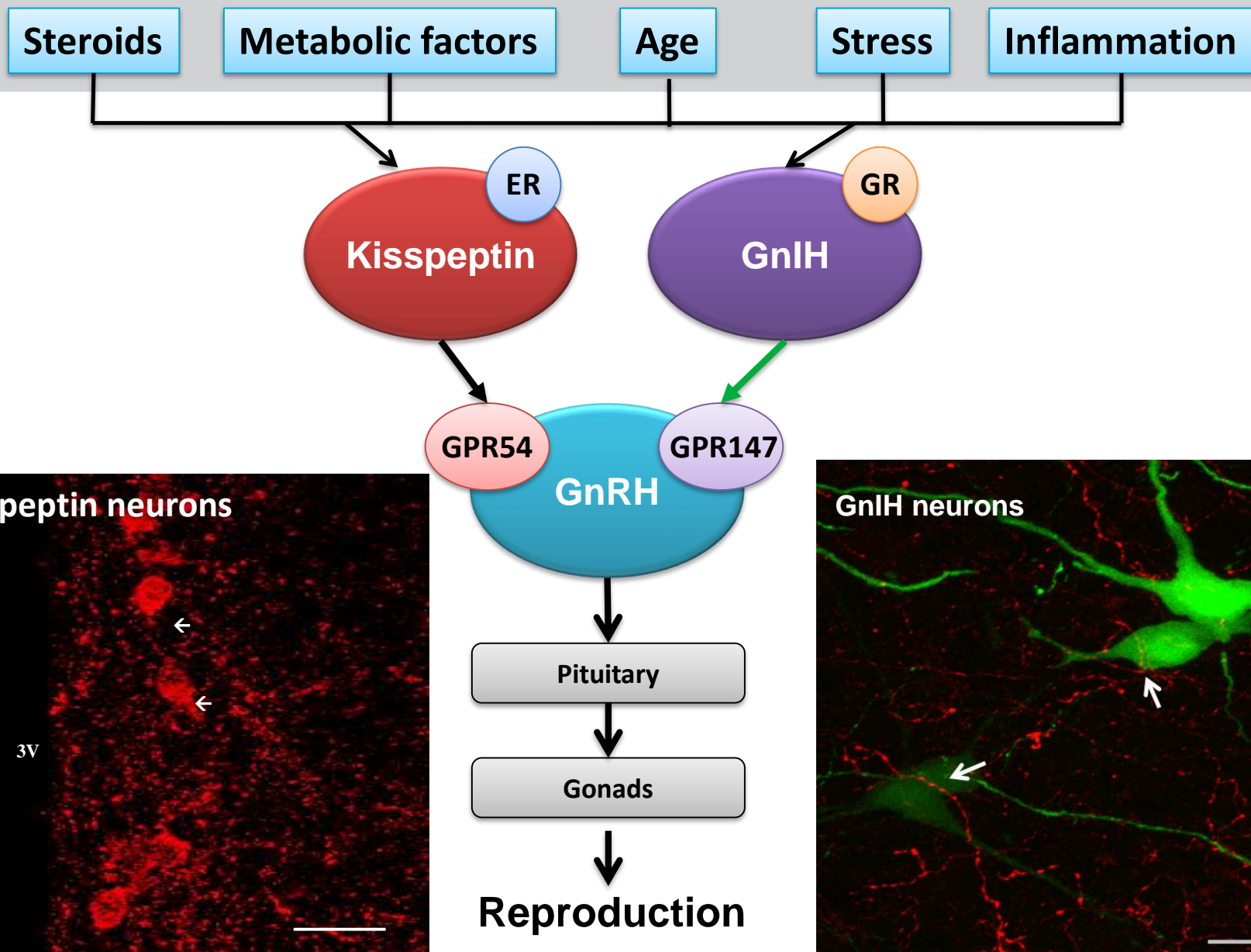


GPR54

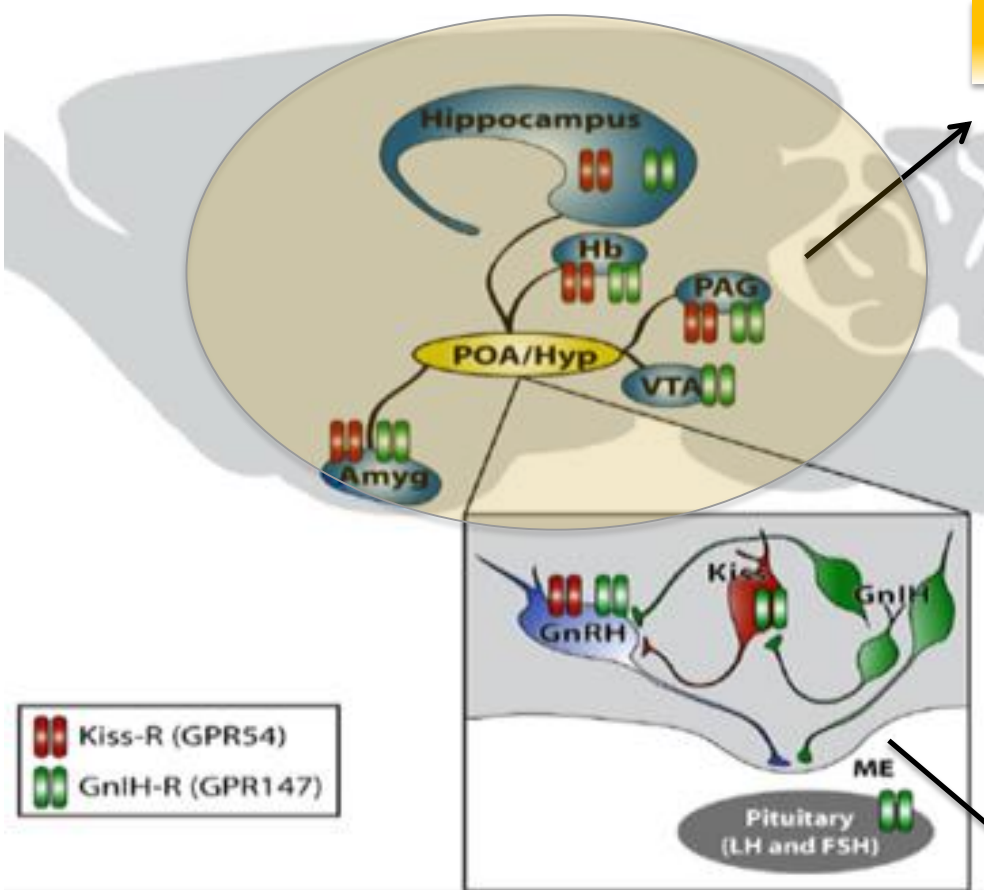
Laser-captured single digoxigenin-labeled neurons of gonadotropin-releasing hormone types reveal a novel G protein-coupled receptor (Gpr54) during maturation in cichlid fish.



PARHAR et al (2004), Endocrinology.



Kisspeptin and GnIH in hippocampus



Cognition, Depression, Emotion

Kisspeptin modulates sexual and emotional brain processing in humans.
J Clin Invest. 2017

Kisspeptin enhances memory and mitigates memory impairment induced by A β 1-42. Neurobiol Learn Mem. 2015

Kisspeptin ? a possible drug-candidate for mental and cognitive disorders.
J Neurol Neurophysiol 2015

Effects of GnIH on Oxytocin Release and Anxiety-Related Behaviour in Rats
Journal of Neuroendocrinology, 2010

Reproduction

Parhar et al (2016) Front. Endocrinol.

HYPOTHALAMIC-PITUITARY-GONADAL AXIS

