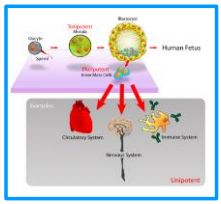
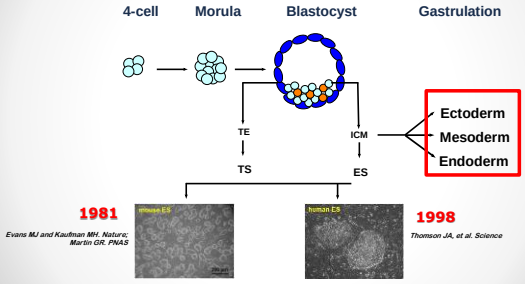
"Development of Neural and Neural Crest Progenitor Cells from Human Pluripotent Stem Cells"



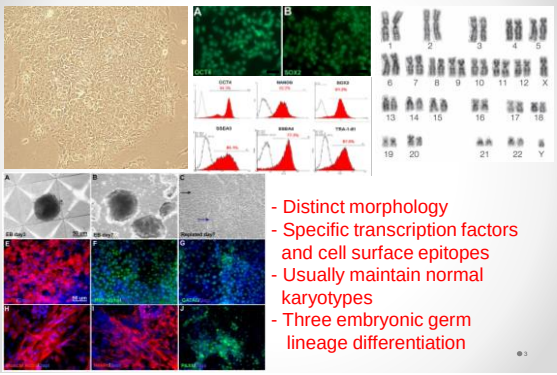
July 23th, 2014

Parinya Noisa, PhD.
Suranaree University of Technology

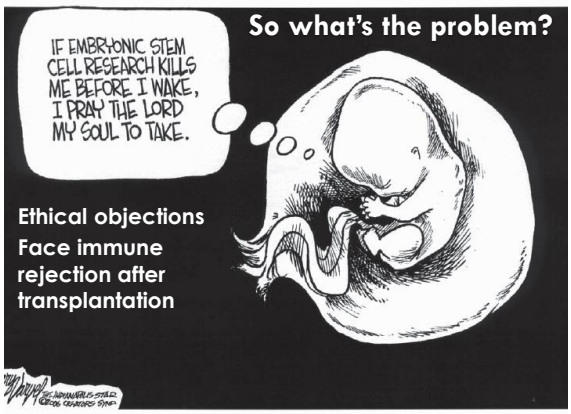
Human Embryonic Stem Cells



Characteristics of Human Embryonic Stem Cells

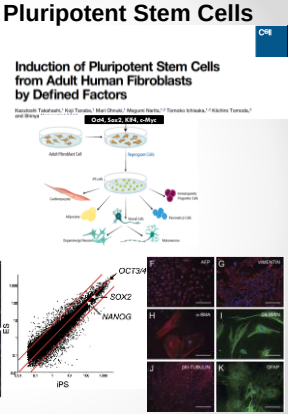


- Distinct morphology
- Specific transcription factors and cell surface epitopes
- Usually maintain normal karyotypes
- Three embryonic germ lineage differentiation

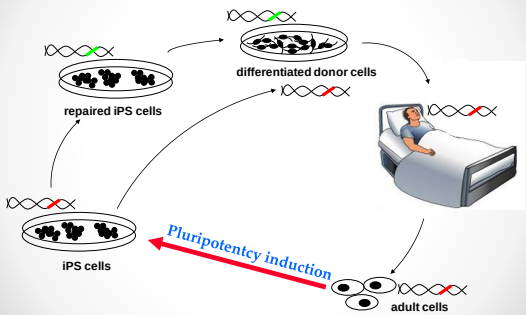


Discovery of Induced Pluripotent Stem Cells

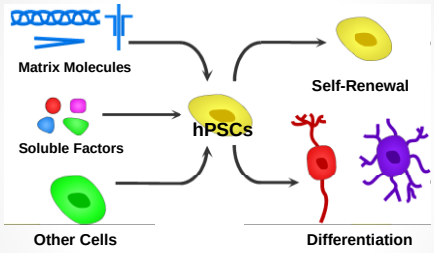
The Shared Nobel Prize in Physiology or Medicine 2012 *"for the discovery that mature cells can be reprogrammed to become pluripotent"*



Patient Specific Induced Pluripotent Stem Cells

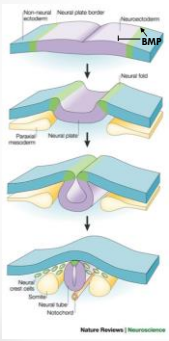


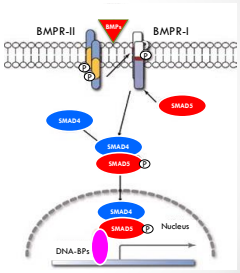
Signals to Stem Cells



Little, et al. Chemical Reviews , 2008

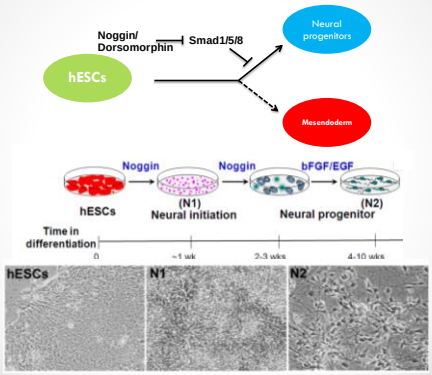
Early Neural Tissue Development



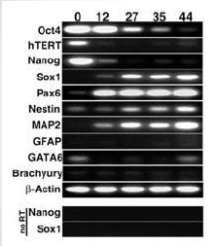


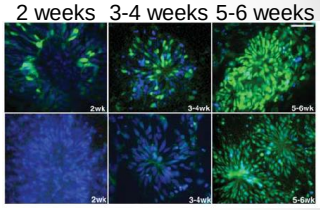
Id1,2,3

Neural Differentiation of hESCs

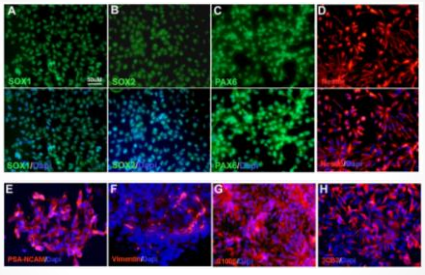


Neural Differentiation of hESCs



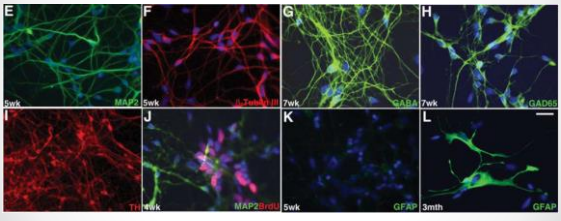


Neural Differentiation of hESCs



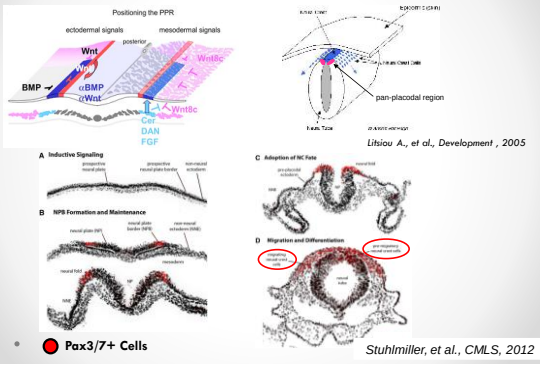
hESC- derived neural progenitor cells express markers for early embryonic neural stem cells – radial glial cells

Differentiation Potential of hESC-Derived Neural Progenitors



GABAergic neurons, Glutaminergic neurons, Glial cells

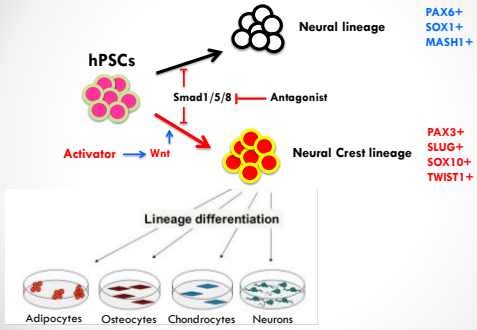
Neural Crest Development



Litsiou A., et al., Development , 2005

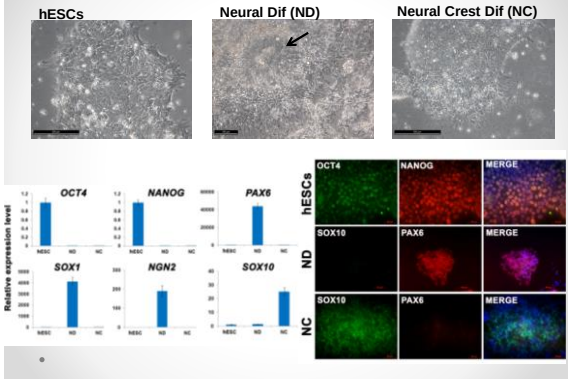
Stuhlmiller, et al., CMLS, 2012

Neural Crest Differentiation from hPSCs

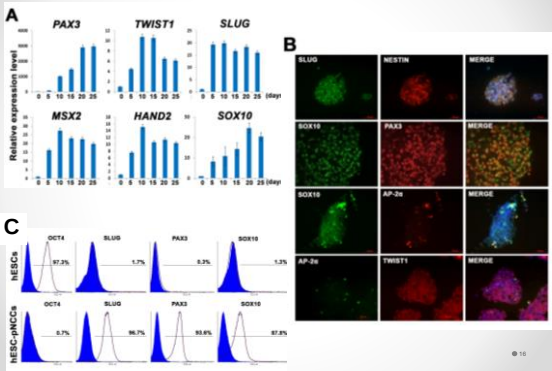


Menedez, et al., PNAS, 2011

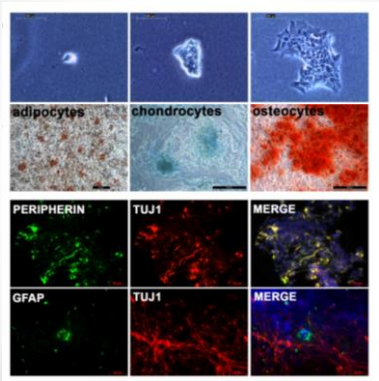
Specificity of Neural Crest Differentiation Protocol



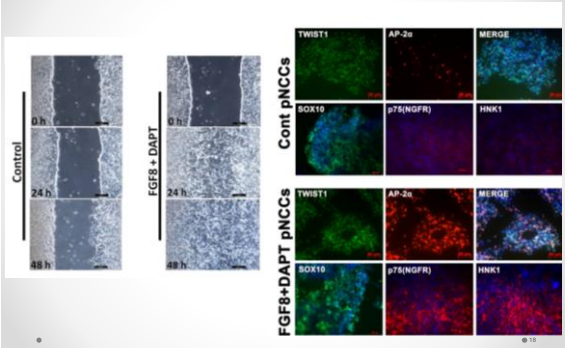
Efficient Protocol to Derive Neural Crest Progenitors



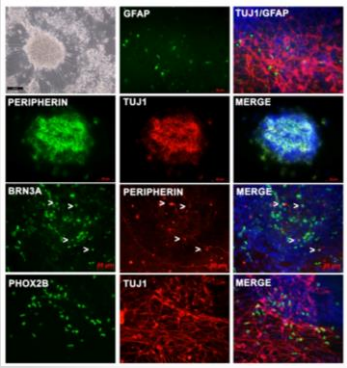
Neural Crest Progenitors are Multipotent



Activation of FGF8 and Inhibition of Notch Induce Migratory NC Phenotypes



Inhibition of Notch Induces NC-Derived Neurons

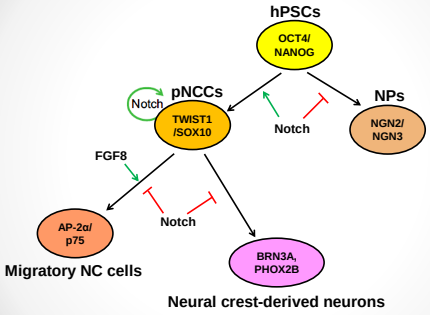


Peripheral neurons

Peripheral sensory neurons

Autonomic neurons

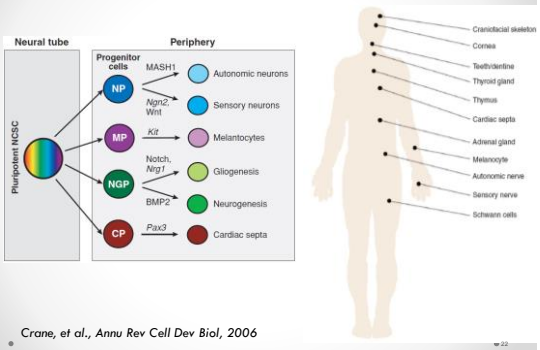
Notch and Neural Crest Differentiation



To sum up…

- Neuraland neural crest stem cells could be efficiently derived from hESCs.
- Both neural and neural crest stem cells could be precursors for various types of neurons
- Robust and efficient protocol for the derivation of premigratory neural crest-like cells (pNCCs)
- pNCCs are multipotent and able to generate neural crest derivative cells, including peripheral sensory neurons.
- Modulation specific signaling pathways could induce migratory neural crest cells and possible other neural crest derivatives.

Challenging of Neural Crest Differentiation



Crane, et al., Annu Rev Cell Dev Biol, 2006

Acknowledgments

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Dr. Ras Trokovic
Dr. Kirmo Wartiovaara
Eila Korhonen

THAILAND
ACADEMY OF FINLAND

END

Modeling neurological disorders by using iPSCs

Disease	Target cell	Potential to be disease model		Drug test
		Successful differentiated into target cell type	Neuronal pathology	
Early-onset neurological disorders				
Fragile X syndrome	ND	ND	Loss of FMR1 expression	ND
Prader-Willi syndrome	Neurons	Yes	Imprint disorder	ND
Rett's syndrome	Neurons	Yes	Loss of synapses, reduced spine density, smaller soma size	Yes
Familial dysautonomia	Neural crest cells	Yes	Loss of neural crest cells	Yes
Friedreich's ataxaia	Motor neuron	Yes	*FXN* gene repression	ND
Angelman's syndrome	Neurons	Yes	Imprint disorder	ND
Down's syndrome	Neuron	ND	ND	ND
Spinal muscular atrophy	Motor neurons	Yes	Loss of neuron formation, loss of *SMN* gene expression	Yes
Late-onset neurological disorders				
Amyotrophic lateral sclerosis (ALS)	Motor neurons	ND	Not shown	ND
Huntington's disease (HD)	Striatal neurons	Yes	Not shown	ND
Parkinson's disease (PD)	Dopaminergic neurons	Yes	Not shown	ND
Alzheimer's disease (AD)	Cholinergic neurons	Yes	Increase ratio of Aβ42 to Aβ40	Yes

[a] ND: not determined.

Kunkanjanawan T., et al., JBB., 2011 25