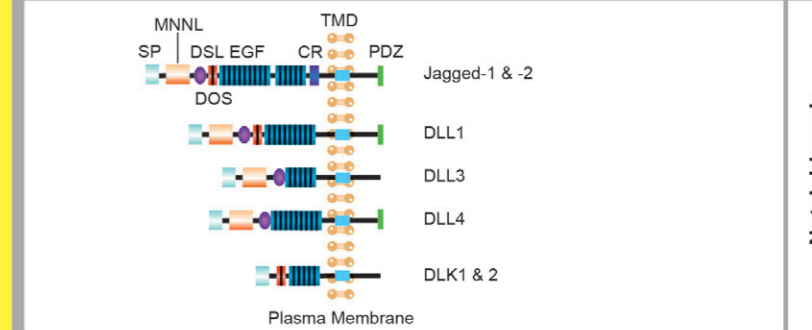
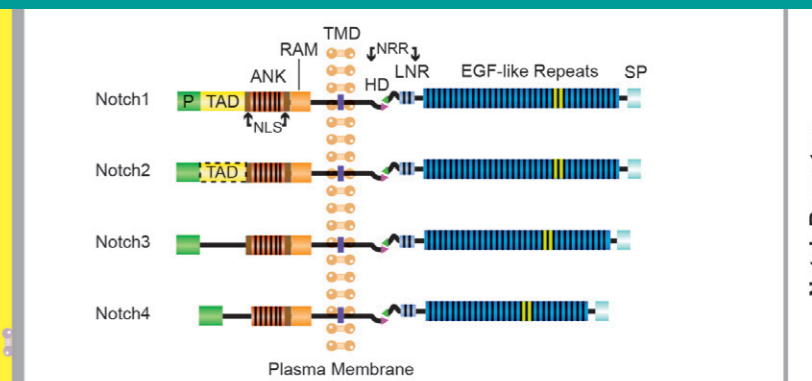
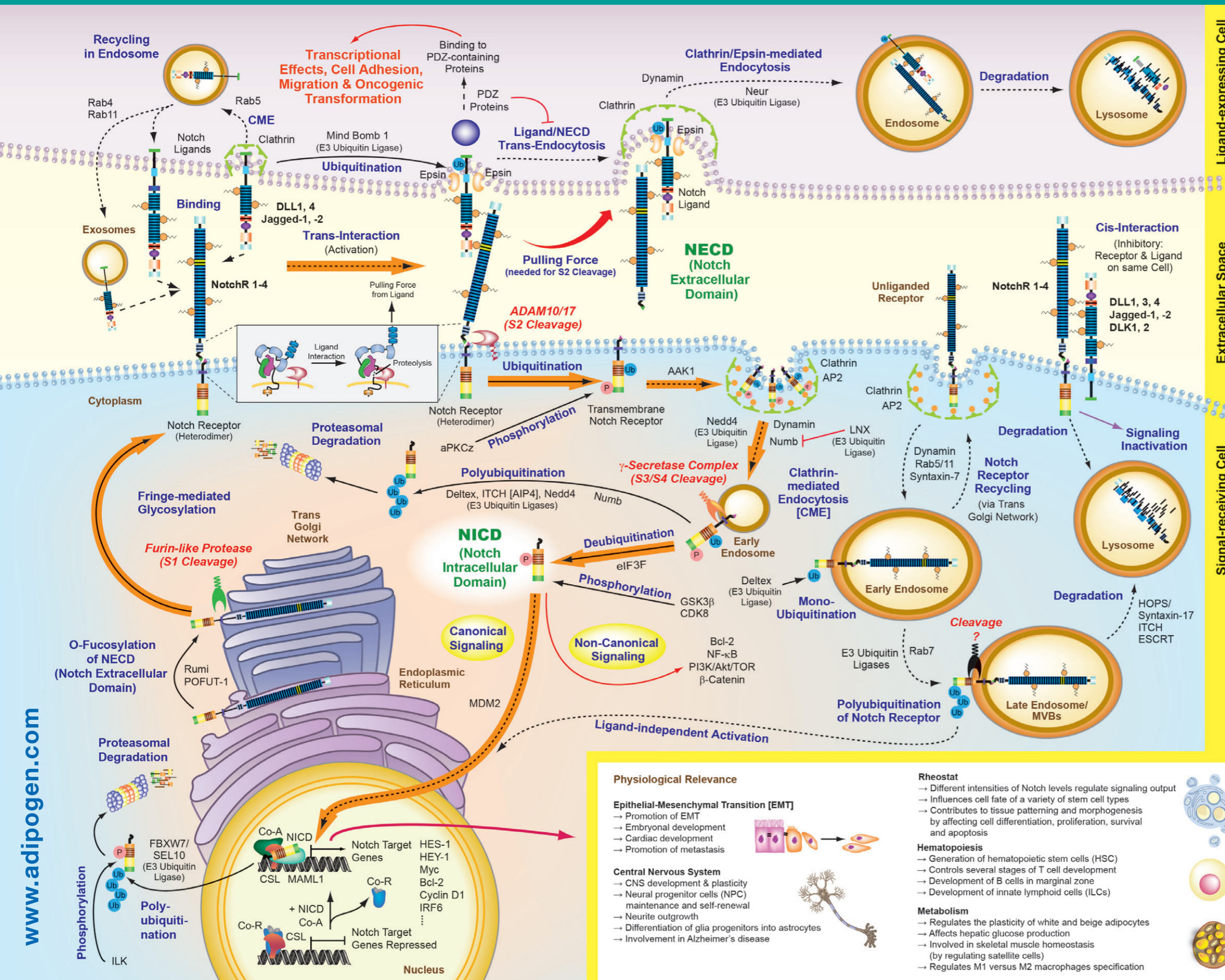


# Notch Signaling Pathway

## Activation, Signaling & Regulation

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ANK: Ankyrin Repeats  
CR: Cysteine-rich Domain  
DOS: Delta and OSM-11-like Proteins Domain  
DSL: Delta, Serrate and LAG-2 Domain  
EGF: Epidermal Growth Factor-like Repeats  
HD: Heterodimerization Domain  
LNR: Cysteine-rich Lin12-Notch Repeats  
NRR: Negative Regulatory Region  
MNL: Module at N-terminal Domain of Notch Ligands

NLS: Nuclear Localization Signal  
P: PEST Domain  
PDZ: PDZ Domain  
RAM: RBPJ-associated Molecule  
SP: Signal Peptide  
TAD: Transactivation Domain  
TMD: Transmembrane Domain

Glycosylation  
 Ubiquitination  
 Phosphorylation  
 Binding  
 Modification  
 Translocation  
 Proteases  
 Notch Canonical Pathway

ADAM: A Disintegrin and Metalloproteinase Domain-containing Protein  
 AP2: Adaptor Protein 2  
 AKK1: AP2-associated Protein Kinase 1  
 eIF3F: Eukaryotic Translation Initiation Factor 3 Subunit F  
 ESCRT: Endosomal Sorting Complexes Required for Transport  
 HOPS: Homotypic Fusion and Vacuole Protein Sorting Complex  
 ILK: Integrin-linked Kinase  
 LNX: Ligand of Numb Protein X  
 MDM2: Murine Double Minute 2  
 MVBs: Multivesicular Bodies  
 Neur: Neutralized  
 S1: Protease Site 1

**Nucleus**  
 Co-A: Co-Activator Proteins  
 Co-R: Co-Repressor Proteins  
 CSL (RBP J): CBF1/Su(H)/Lag-1 Complex  
 MAML1: Mastermind-like 1

### Physiological Relevance

**Epithelial-Mesenchymal Transition [EMT]**

- Promotion of EMT
- Embryonal development
- Cardiac development
- Promotion of metastasis

**Central Nervous System**

- CNS development & plasticity
- Neural progenitor cells (NPC) maintenance and self-renewal
- Neurite outgrowth
- Differentiation of glia progenitors into astrocytes
- Involvement in Alzheimer's disease

**Rheostat**

- Different intensities of Notch levels regulate signaling output
- Influences cell fate of a variety of stem cell types
- Contributes to tissue patterning and morphogenesis by affecting cell differentiation, proliferation, survival and apoptosis

**Hematopoiesis**

- Generation of hematopoietic stem cells (HSC)
- Controls several stages of T cell development
- Development of B cells in marginal zone
- Development of innate lymphoid cells (ILCs)

**Metabolism**

- Regulates the plasticity of white and beige adipocytes
- Affects hepatic glucose production
- Involved in skeletal muscle homeostasis (by regulating satellite cells)
- Regulates M1 versus M2 macrophages specification

**Cancers**

- T cell acute lymphoblastic leukemia (T-ALL)
- B cell lymphoproliferative disorders
- Other hematological malignancies
- Brain tumors including gliomas and medulloblastomas
- Solid tumors in liver, breast, bladder, lung, prostate and other organs
- Melanomas
- Colorectal tumors
- Regulates survival and renewal of cancer stem cells

**Angiogenesis/Heart**

- Control of the sprouting pattern of blood vessels
- Pivotal regulator of tumor angiogenesis and vascular development
- Crucial in heart development
- Congenital heart defects such as bicuspid aortic valve diseases
- Cerebral autosomal dominant arteriopathy with subcortical infarct and leukoencephalopathy