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COURSE: NEUROANATOMY

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ASSIGNMENT TITLE: CEREBELLUM AND ITS CONNECTIONS

**ASSIGNMENT**

Write a concise review on the developmental genetics of the cerebellum and highlight the genetic bases of known cerebellar disorders

**ANSWER**

The internal structure of the cerebellum reflects an interesting paradox, in that the cellular arrangement is simple and repeated throughout YET its neuronal connections are wired in a complex array of gene expression domains and functional circuits. The developmental mechanism that regulates the development of cerebellar structures and circuitry provides a powerful example/model for how the brain networks are formed.

Two primary germinal zone generate cells that make up of cerebellum. Each zone expresses specific set of genes that give rise to cell lineages within the cerebellar primordium, then groups of differentiated projection neuron and interneuron progenitors migrate into the developing cerebellum. After this, a number of patterning events occur including the following:

* Transformation of smooth cerebellar surface into patterned series of folds.
* Formation of three distinct cellular layers.
* Demarcation of parasagittal gene expression domains.

Together, these structural and molecular organizations are thought to support the connectivity between incoming AFFERENT NEURONS and their TARGET CELLS.

AFTER BIRTH; genetic programs and neuronal activity repattern synaptic connections into MODULES (Topographic Neuronal Network (TNN)), which are organized around a longitudinal zone plan.

Some genes when mutated cause disruptions in cerebellar development which results in cerebellar disorders/malformations and they are as follows:

* CEREBELLAR VERMIS HYPOPLASIA (CVH):

Implicated human gene: OPHN1

Likely process disrupted: Spine morphogenesis.

* DANDY-WALKER MALFORMATION (DWM):

Implicated human genes: ZIC1, ZIC4, FOXC1

Likely process disrupted: Granule cell differentiation.

* JOUBERT SYNDROME AND RELATED DISORDERS (JSRD):

Implicated human genes: AHI1, ARL13B, CCD2A, CEP290, INPP5E, NPHP1, RPGRIP1L & TMEM67

Likely process disrupted: Granule cell proliferation.

* PONTOCEREBELLAR HYPOPLASIA (PCH):

Implicated human genes: CASK, RARS2, TSEN54, TSEN34, TSEN2

Likely processes disrupted: Spine development, cell proliferation, tRNA splicing, cellular maintenance.