Genetic determination of body plan in development

Trivially we are all living in **3 spatial dimensions**. So the body has to develop along **three axes**: **cranio-caudal** (also called antero-posterior), **dorso-ventral** and **right-left**.

Let´s use the craniocaudal axis for a simplified illustration of the processes involved. Cells from the epiblast (upper, ectodermal plate of the embryo) migrate down (“ingress”) through the primitive streak in the middle to form the mesoderm. **Cells migrating sooner** are forming the more cranial region while cells migrating later form more caudal region. Prior to ingression, epiblast cells start to express Hox (homeobox) genes. **Hox genes** are found in four clusters (clusters A-D, in ech there are genes 1-13, with few gaps). In each cluster individual Hox genes are arranged in the same order, in which they are gradually turned on in epiblast cells before moving into mesoderm. Therefore the first most cranial cells express the first Hox gene, next cell wave express first and second, etc., until the last cells are expressing all Hox genes. Expression pattern along the body axis is thus collinear with the gene position in DNA (collinearity rule). The most posterior Hox gene expressed in the region is specifying what will happen (posterior prevalence). Hox genes then do not directly influence proliferation or differentiation of any particular tissue, but they specify the morphology of the whole segment. If a Hox gene is lost, the more cranial Hox genes are still expressed in the critical segment, which leads to transformation of the segment to more anterior morphology, e.g. transformation of lumbar vertebra into thoracic (including ribs). This is called anterior homeotic transformation (there lays the origin of the name for the genes). Vice versa, posterior homeotic transformation occurs when a gene is overexpressed (and its expression thus starts earlier). In human, the true homeotic mutations are **rare**, since Hox genes of the same number from different clusters (paralogs) can usually compensate the loss of the single gene.