

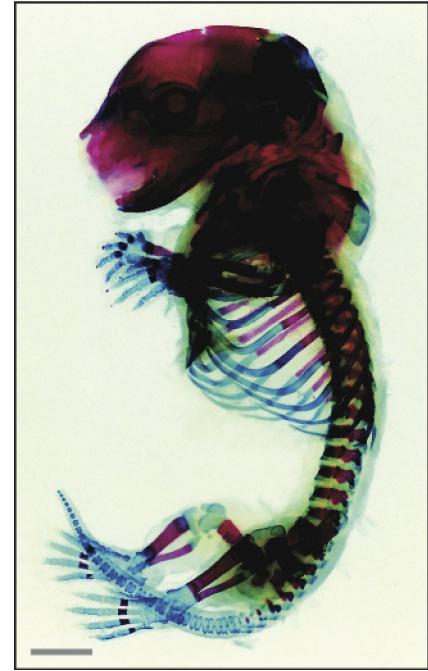
Model organisms and developmental biology

仲寒冰

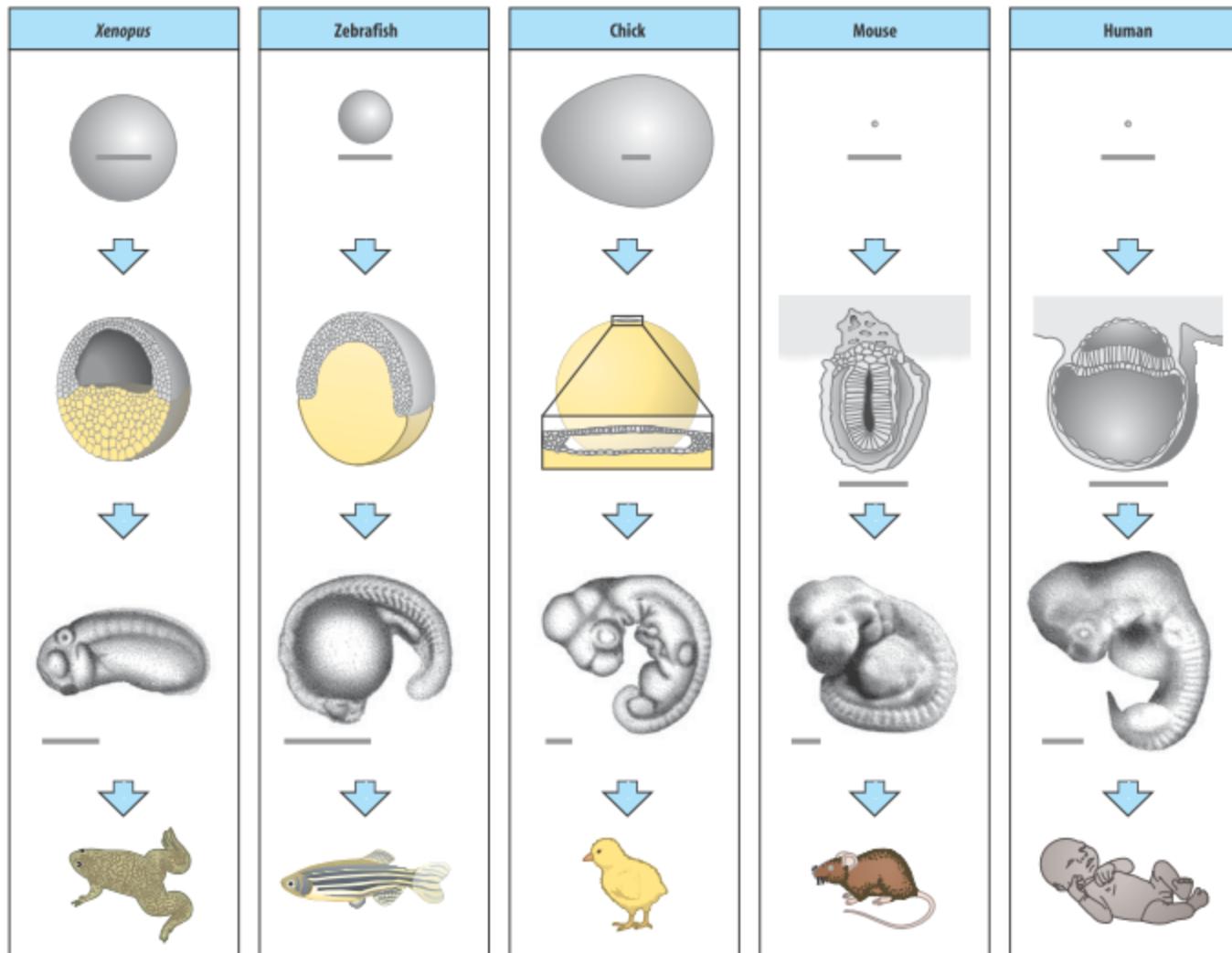
zhong.hb@sustc.edu.cn

Vertebrate body plan

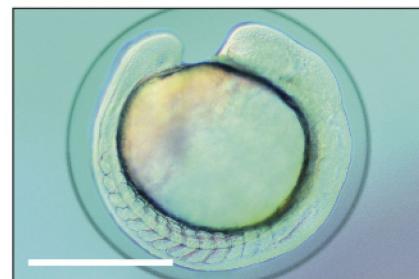
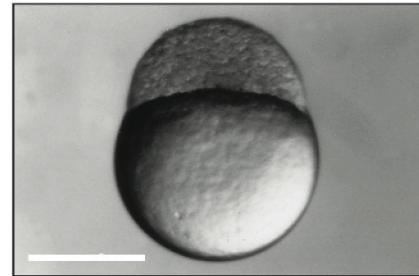
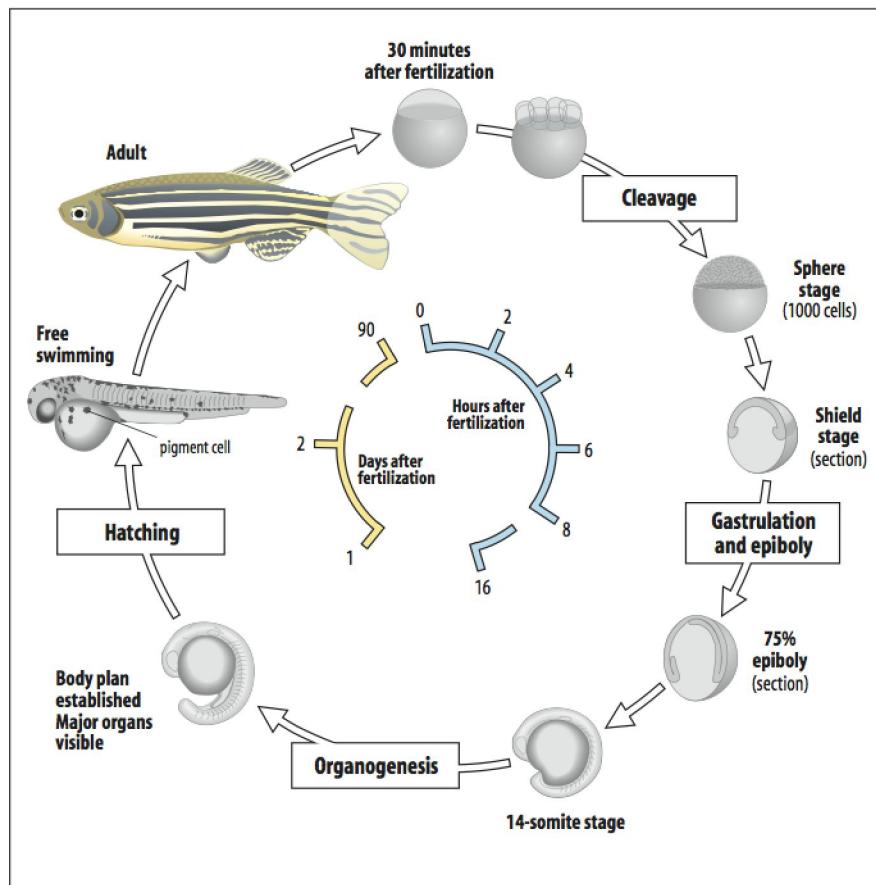
- 1. Vertebral column surrounding the spinal cord.
- 2. Head is at the anterior end within skull.
- 3. Paired appendages and post-anal tail.
- 4. Spinal cord is on dorsal side.

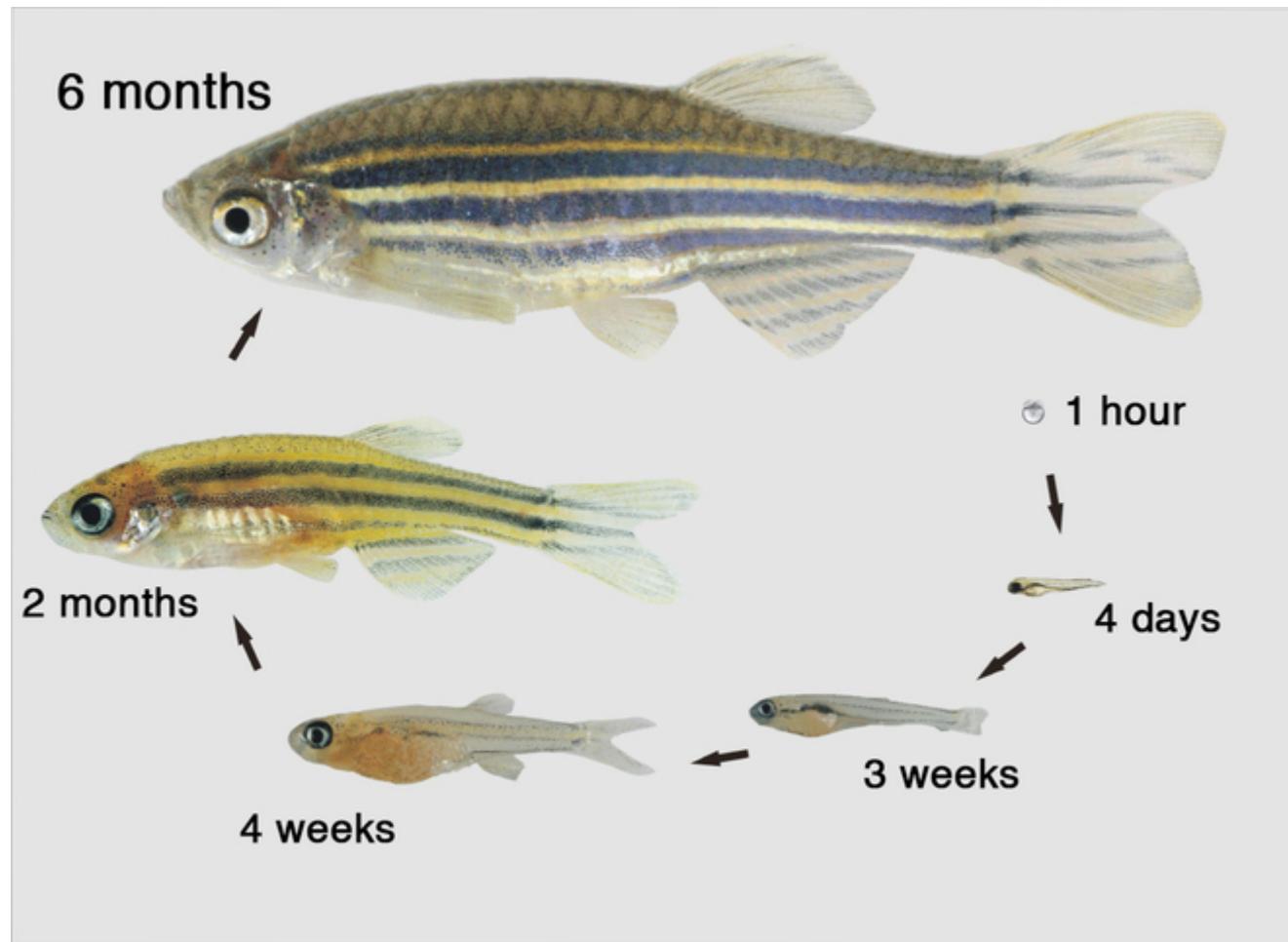


A 17.5-day mouse embryo

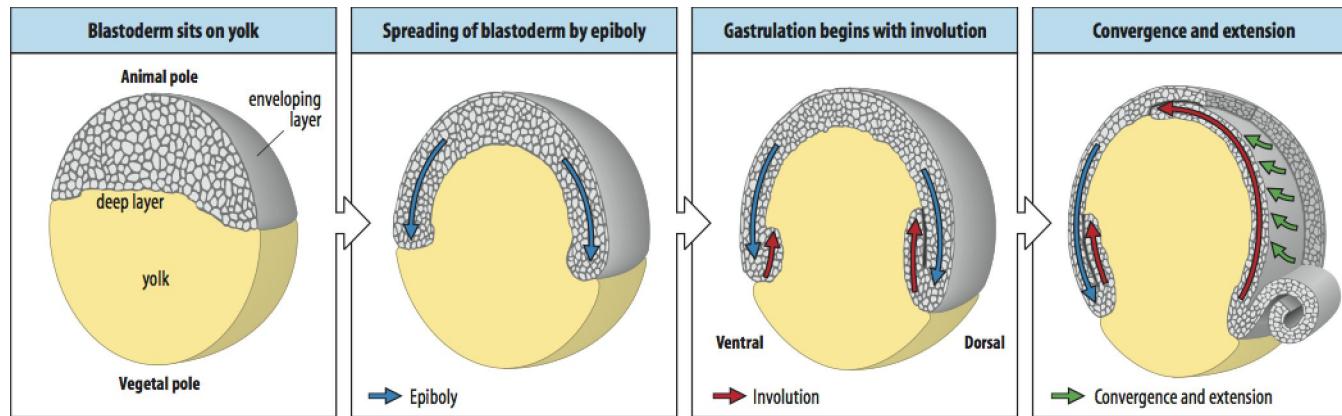
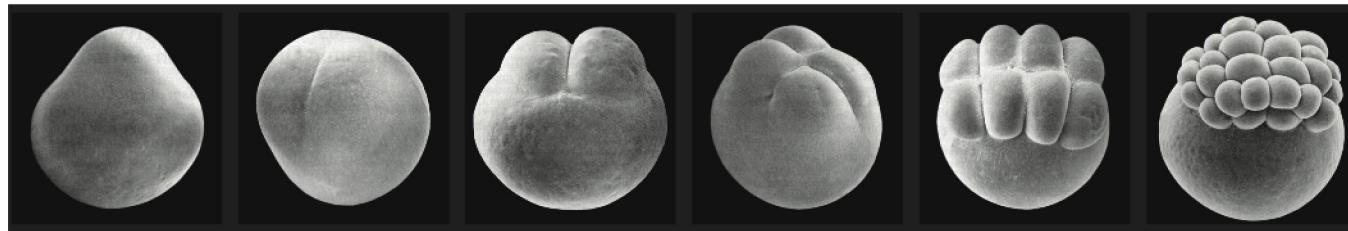


Life cycle of the zebrafish

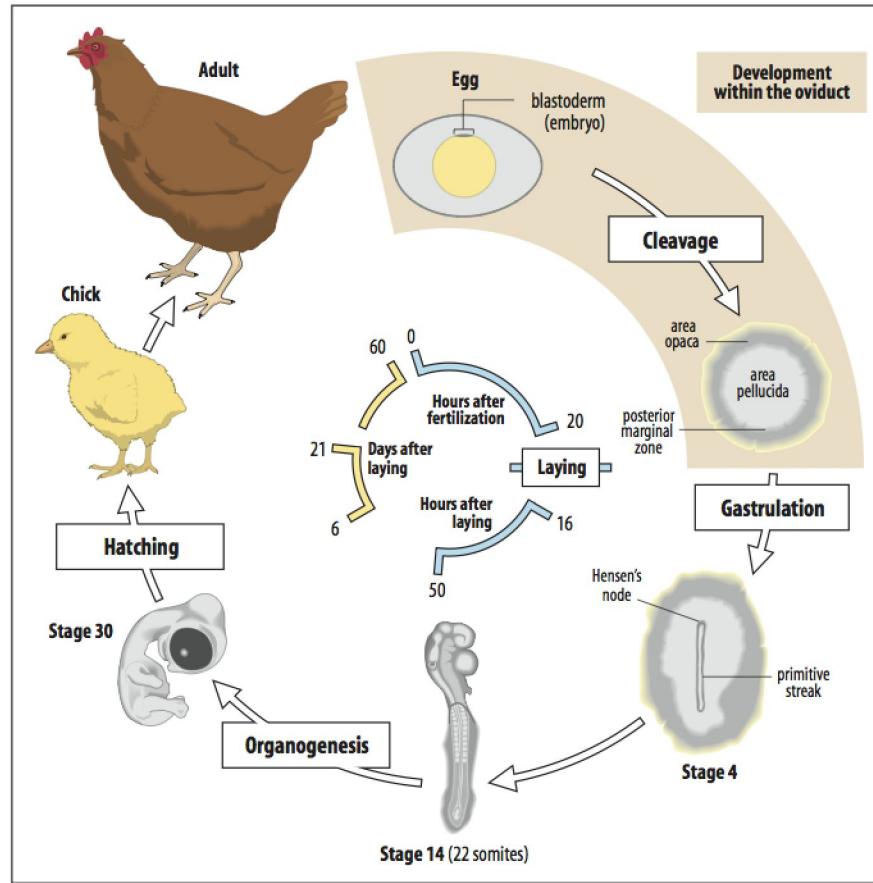
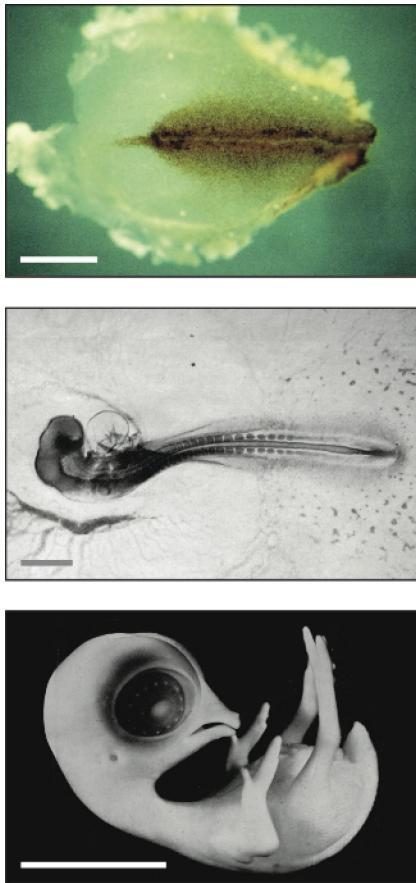




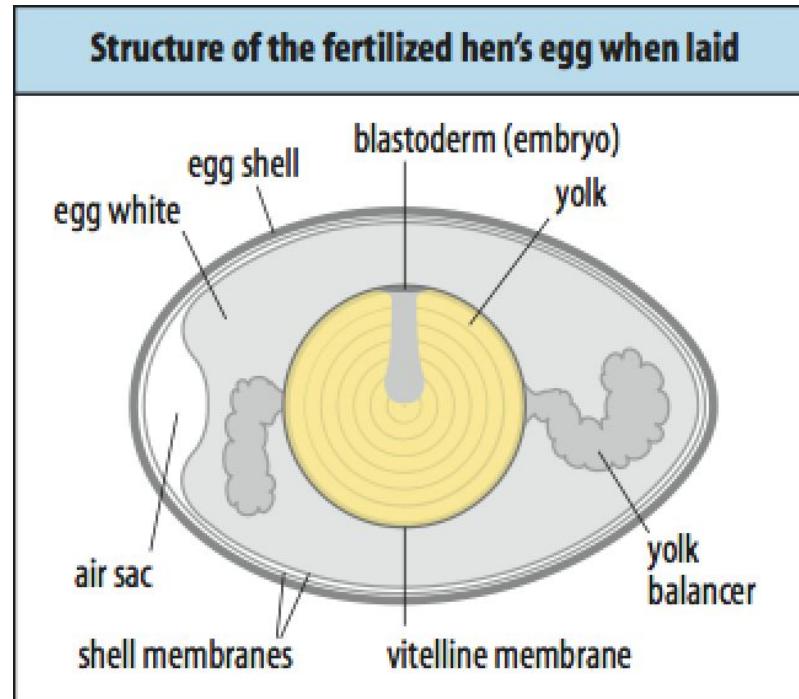
Cleavage and epiboly of the zebrafish embryo



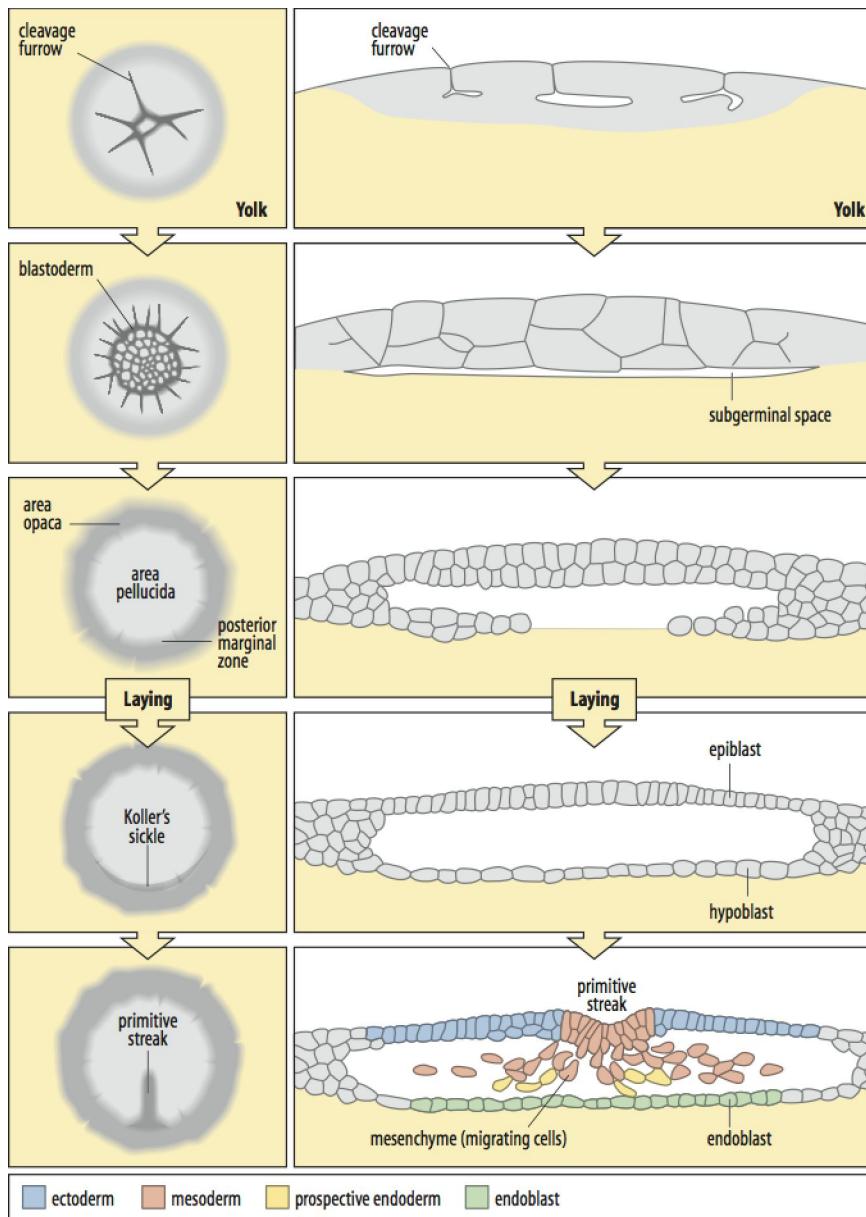
Life cycle of the chicken



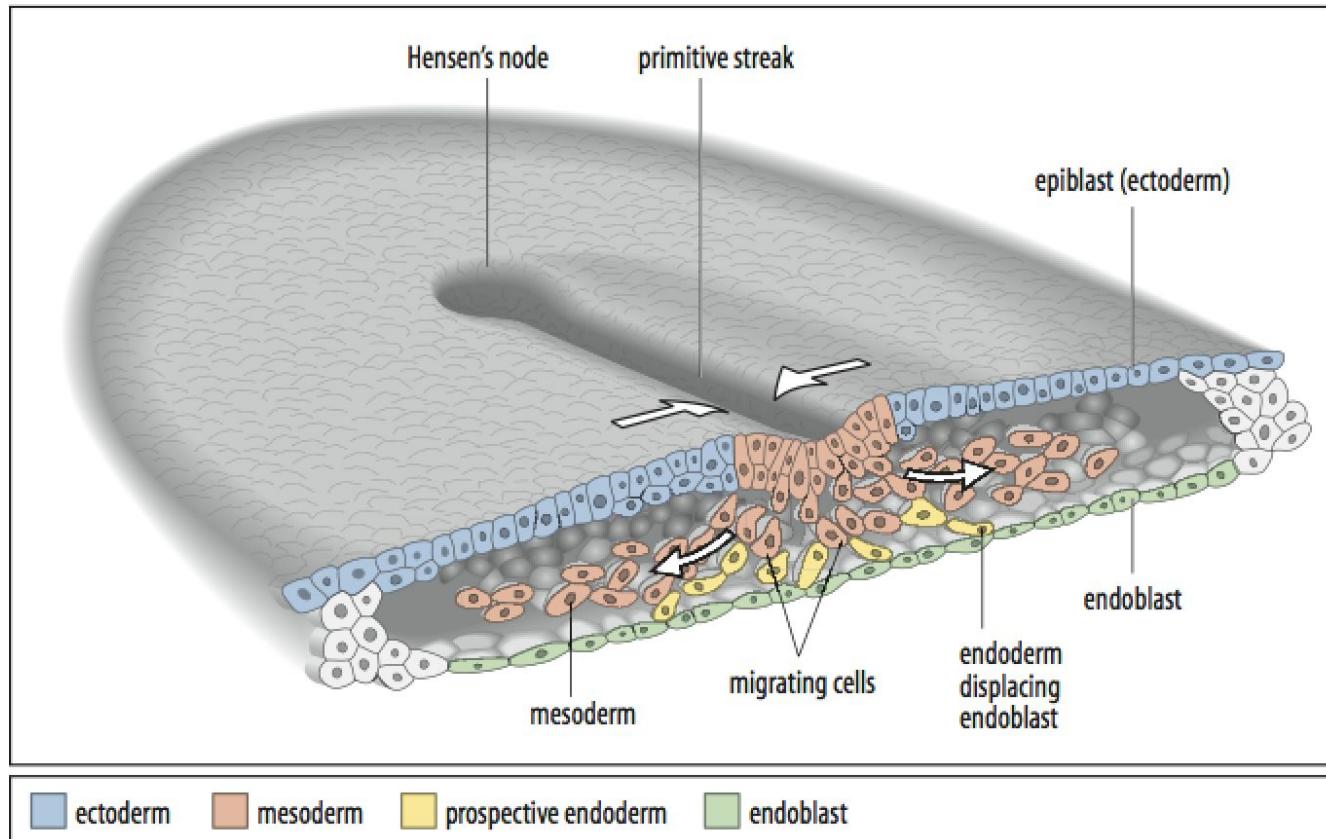
The structure of a hen's egg at the time of laying



Cleavage and epiblast formation in the chick embryo

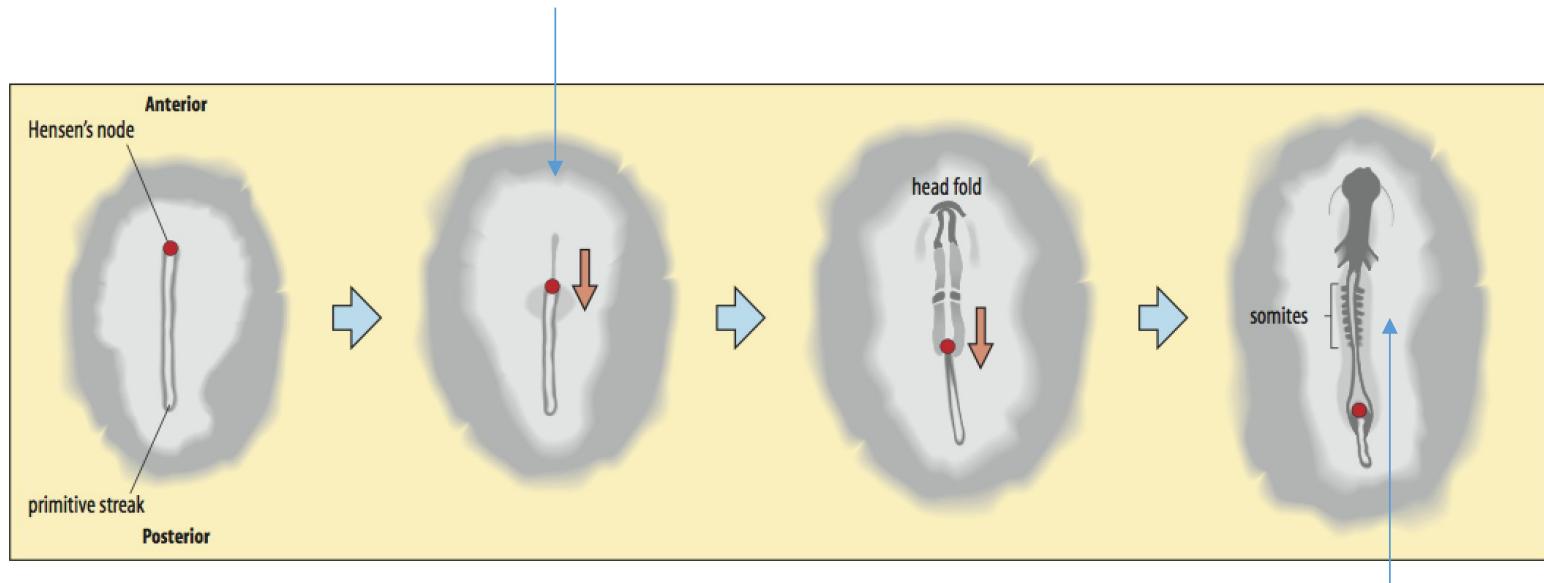


Ingression of mesoderm and endoderm during gastrulation

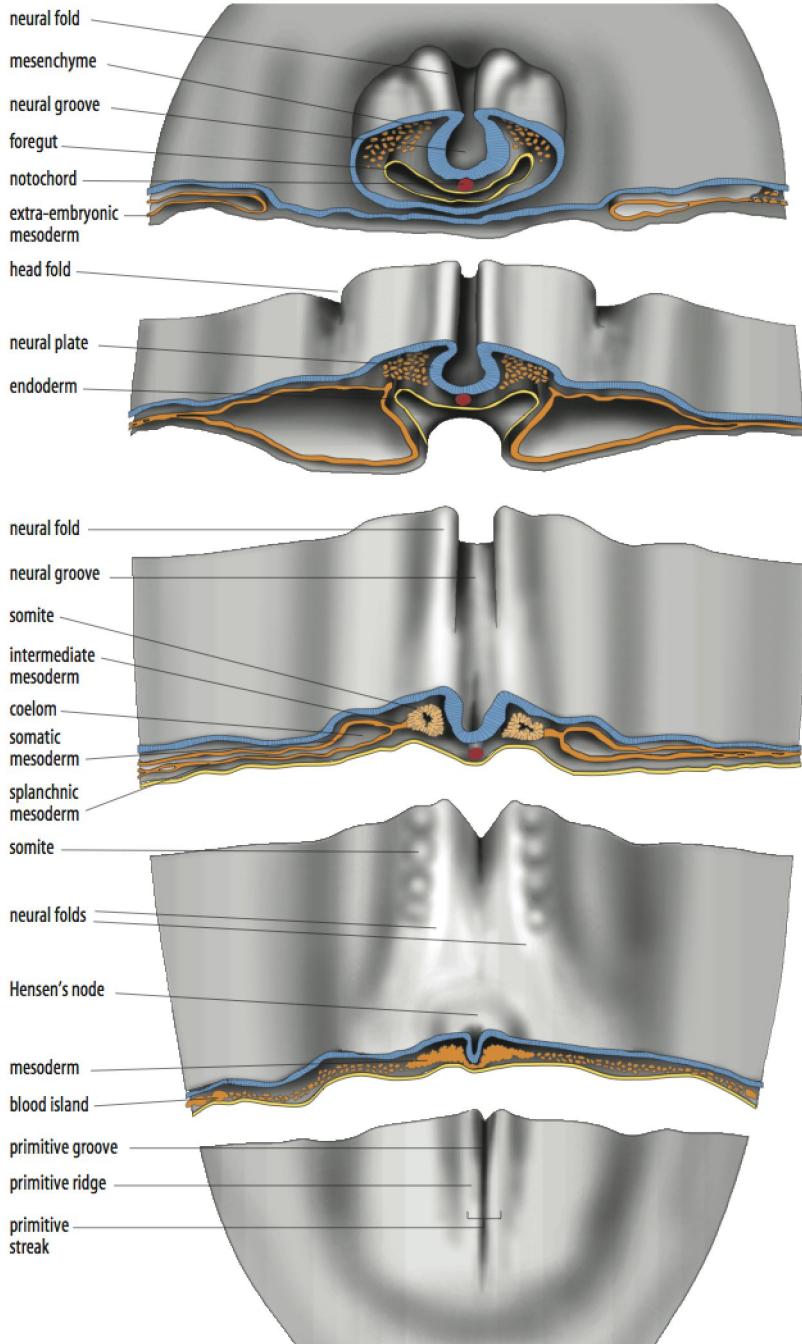


Regression of Hensen's node

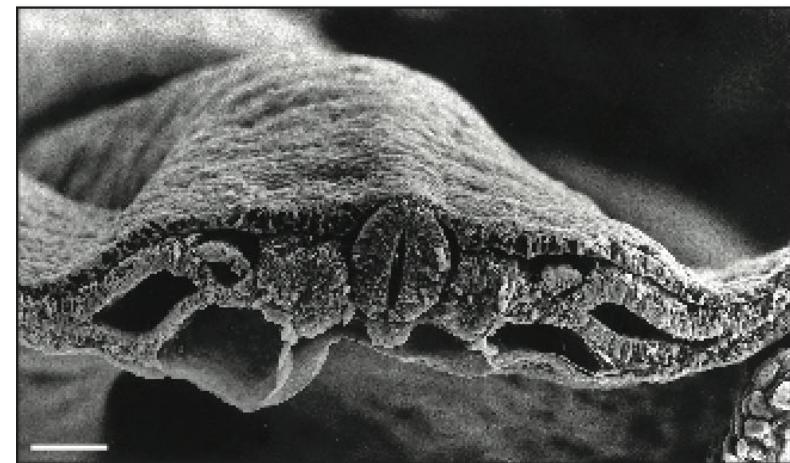
Prechordal plate mesoderm and head process (head notochord)



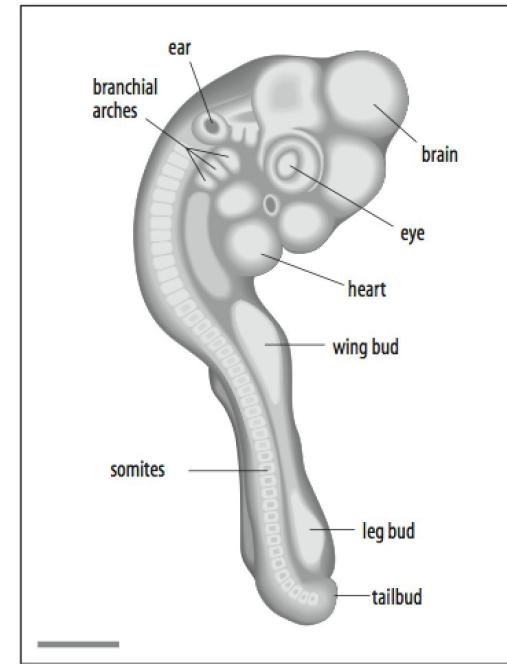
Lateral plate mesoderm
(heart, kidneys, blood,
and vascular system)



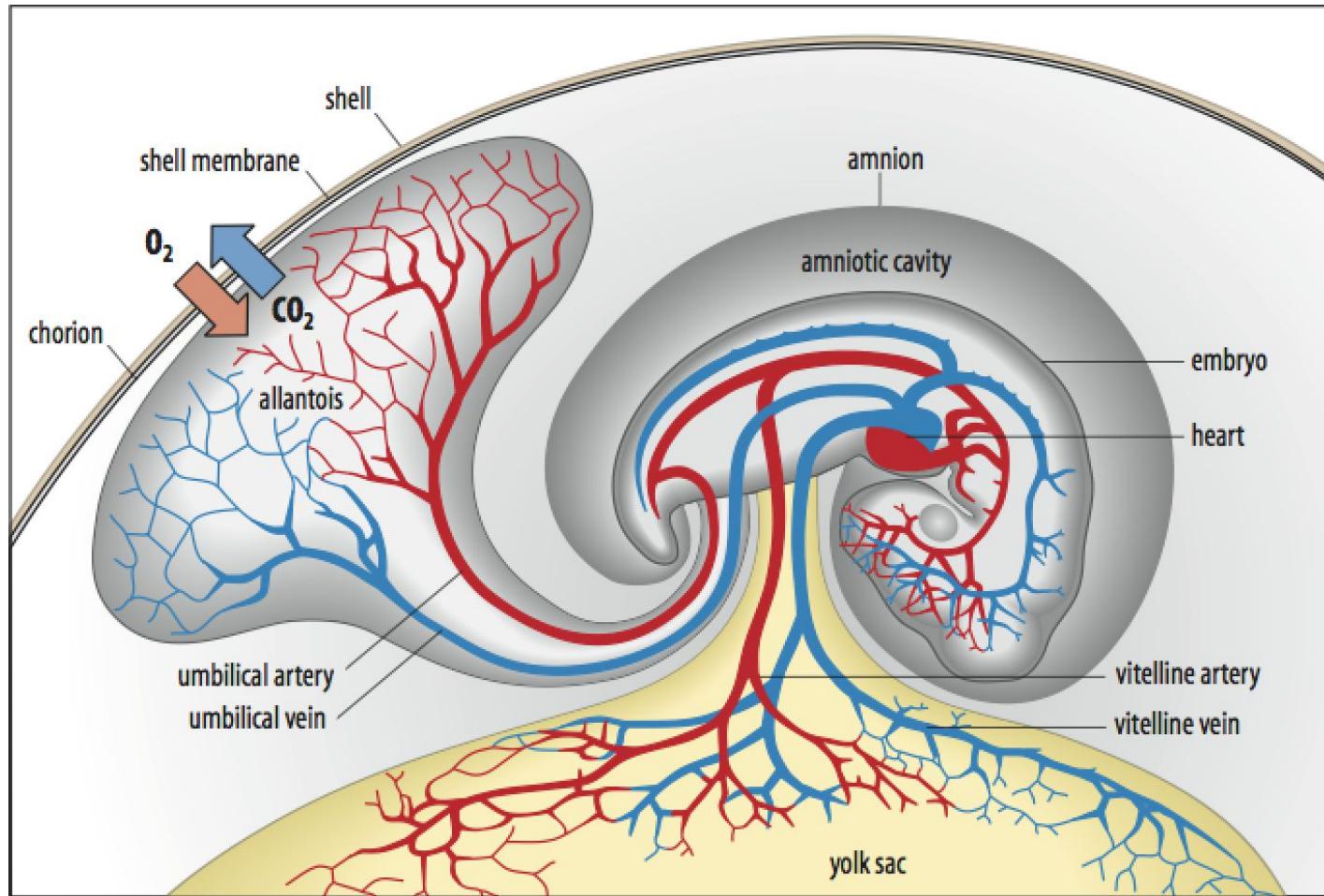
Formation of the neural tube and mesoderm

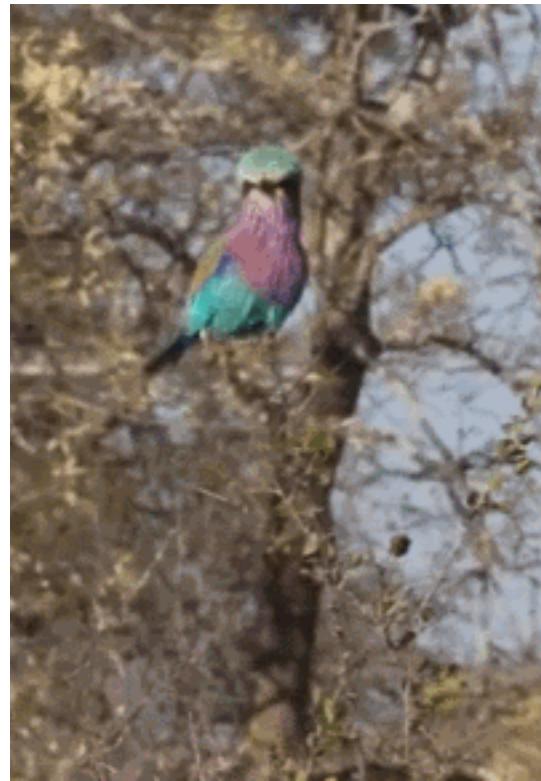


Development of the head region



The extra-embryonic structures and circulation of the chick embryo





Mouse, from pet to model organism

- 1900, Abbie Lathrop moved to Granby MA to raise “fancy” mice and rats. The mouse farm.
- William Ernest Castle (1867-1962), a pioneer in mammalian genetics who was among the first to realize the potential power of mouse models for human disease, bought some of Lathrop's mice for his laboratory in 1902, a fertile time for genetic research immediately after the rediscovery of the now-famous pea experiments of the monk Gregor Mendel.
- Castle and his colleagues had raised inbred strains (Brother-sister mating, 20 generations). Highly homozygous in all loci.
- On Ensembl, 17 key mouse strains were sequenced. The most popular strain, C57BL/6J.

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- William Ernest Castle (1867-1962), a pioneer in mammalian genetics, realized the potential of mice as disease models for human diseases. He conducted his laboratory in his basement and immediately began breeding pea experiments on mice.
- Castle and his wife, Ethel (Brother-sister pair) developed many homozygous strains of mice.
- On Ensembl, 17 key mouse strains were sequenced. The most popular strain, C57BL/6J.



Acknowledgement

侯宇的BLOG

生命之初---CSH小鼠分子胚胎课侧记2

http://blog.sina.com.cn/s/blog_5462dedd0100ifyo.html

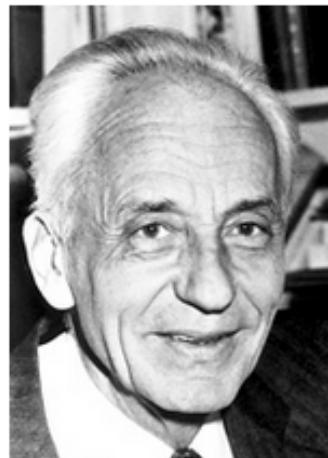


The Nobel Prize in Physiology or Medicine 1980
Baruj Benacerraf, Jean Dausset, George D. Snell

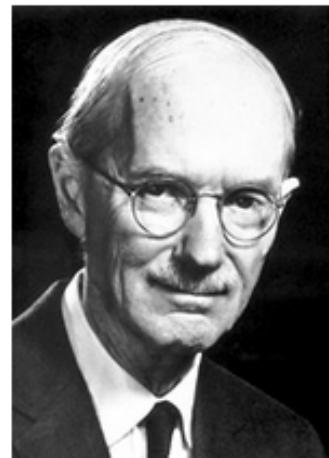
The Nobel Prize in Physiology or Medicine 1980



Baruj Benacerraf



Jean Dausset



George D. Snell

The Nobel Prize in Physiology or Medicine 1980 was awarded jointly to Baruj Benacerraf, Jean Dausset and George D. Snell *"for their discoveries concerning genetically determined structures on the cell surface that regulate immunological reactions"*.

Forward-genetics analysis of sleep in randomly mutagenized mice

Hiromasa Funato^{1,2}, Chika Miyoshi^{1*}, Tomoyuki Fujiyama^{1*}, Takeshi Kanda^{1*}, Makito Sato^{1,3*}, Zhiqiang Wang¹, Jing Ma¹, Shin Nakane⁴, Jun Tomita⁴, Aya Ikkyu¹, Miyo Kakizaki¹, Noriko Hotta-Hirashima¹, Satomi Kanno¹, Haruna Komiya¹, Fuyuki Asano¹, Takato Honda¹, Staci J. Kim¹, Kanako Harano¹, Hiroki Muramoto¹, Toshiya Yonezawa¹, Seiya Mizuno⁵, Shinichi Miyazaki¹, Linzi Connor¹, Vivek Kumar^{6,7}, Ikuo Miura⁸, Tomohiro Suzuki⁸, Atsushi Watanabe⁹, Manabu Abe¹⁰, Fumihiro Sugiyama⁵, Satoru Takahashi⁵, Kenji Sakimura¹⁰, Yu Hayashi^{1,11}, Qinghua Liu^{1,12}, Kazuhiko Kume⁴, Shigeharu Wakana⁸, Joseph S. Takahashi^{1,6,13} & Masashi Yanagisawa^{1,3,13,14}

Sleep is conserved from invertebrates to vertebrates, and is tightly regulated in a homeostatic manner. The molecular and cellular mechanisms that determine the amount of rapid eye movement sleep (REMS) and non-REMS (NREMS) remain unknown. Here we identify two dominant mutations that affect sleep and wakefulness by using an electroencephalogram/electromyogram-based screen of randomly mutagenized mice. A splicing mutation in the *Sik3* protein kinase gene causes a profound decrease in total wake time, owing to an increase in inherent sleep need. Sleep deprivation affects phosphorylation of regulatory sites on the kinase, suggesting a role for SIK3 in the homeostatic regulation of sleep amount. *Sik3* orthologues also regulate sleep in fruitflies and roundworms. A missense, gain-of-function mutation in the sodium leak channel NALCN reduces the total amount and episode duration of REMS, apparently by increasing the excitability of REMS-inhibiting neurons. Our results substantiate the use of a forward-genetics approach for studying sleep behaviours in mice, and demonstrate the role of SIK3 and NALCN in regulating the amount of NREMS and REMS, respectively.

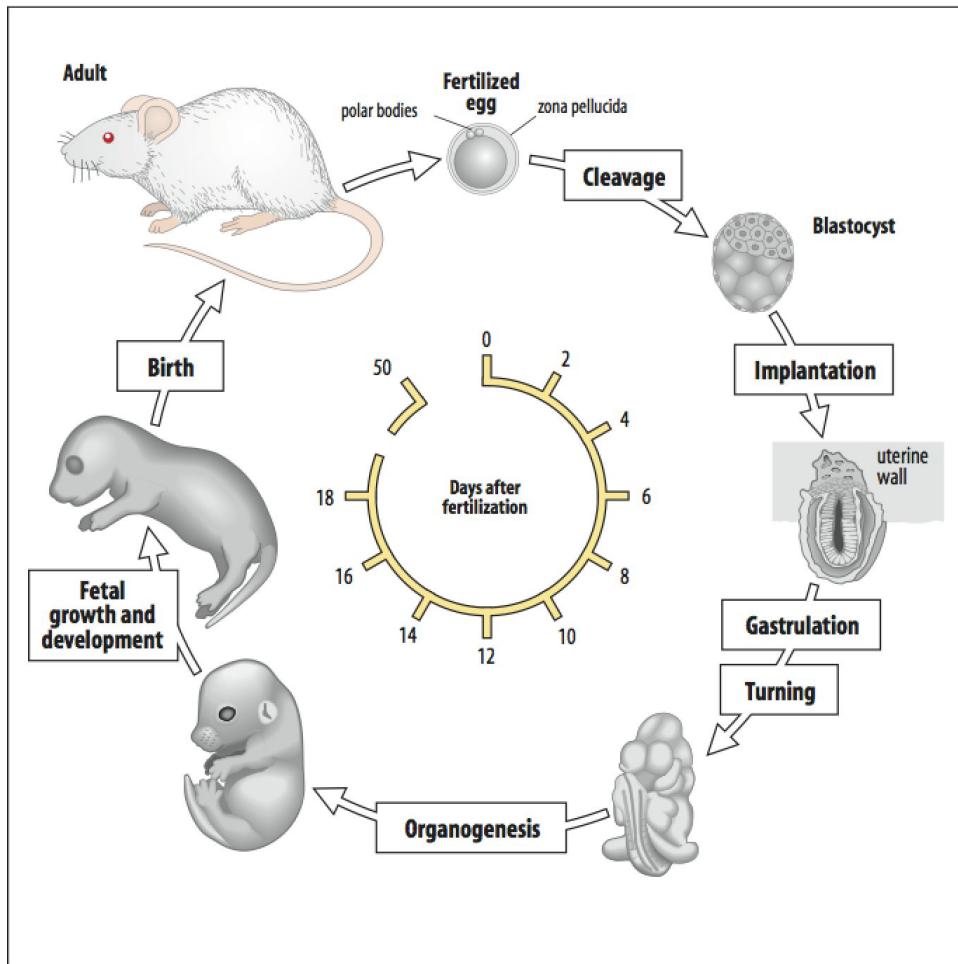
Sleep is an animal behaviour ubiquitously conserved from vertebrates to invertebrates, including flies and nematodes^{1–3}, and is tightly regulated in a homeostatic manner. Sleep in mammals exhibits the cycles of REMS and NREMS that are defined by characteristic activity of electroencephalogram (EEG) and electromyogram (EMG). Time spent in sleep is determined by a homeostatic sleep need, a driving force for sleep/wakefulness switching, which increases during wakefulness and dissipates during sleep^{4,5}. The spectral power in the delta-range frequency (1–4 Hz) of EEG during NREMS has been regarded as one of best markers for the current level of sleep need. Conversely, the level of arousal is positively correlated with sleep latency, which can be regulated independently of sleep need⁶, reflecting the overall activity of wake-promoting neurons. Traditional approaches to locate the neural circuits regulating sleep and wakefulness behaviour included local ablation of brain regions^{7–9}. Recent advances in optogenetic and chemogenetic research have directly demonstrated that switching between sleep and wake states is executed by subsets of neurons in

and mice successfully uncovered the molecular network of the core clock genes regulating circadian behaviours^{17–19}. Sleep-regulating genes were also discovered through the screening of mutagenized flies^{1,2}. However, genetic studies for sleep using mice has been challenging because of the effective compensation and redundancy in the regulation of sleep and wakefulness, and the need for EEG and EMG monitoring of the staging of wakefulness, NREMS and REMS.

Sik3 splice mutation increases NREMS

We induced random point mutations into C57BL/6J (B6J) male mice (G_0) by ethylnitrosourea (ENU) and screened more than 8,000 heterozygous B6J \times C57BL/6N (B6N) F_1 mice for dominant sleep and wakefulness abnormalities through EEG/EMG-based sleep staging (Extended Data Fig. 1a). B6N was chosen as a counter strain because its sleep and wakefulness parameters are highly similar to B6J (Extended Data Fig. 1b), and the entire list of single nucleotide polymorphisms has recently become available²⁰.

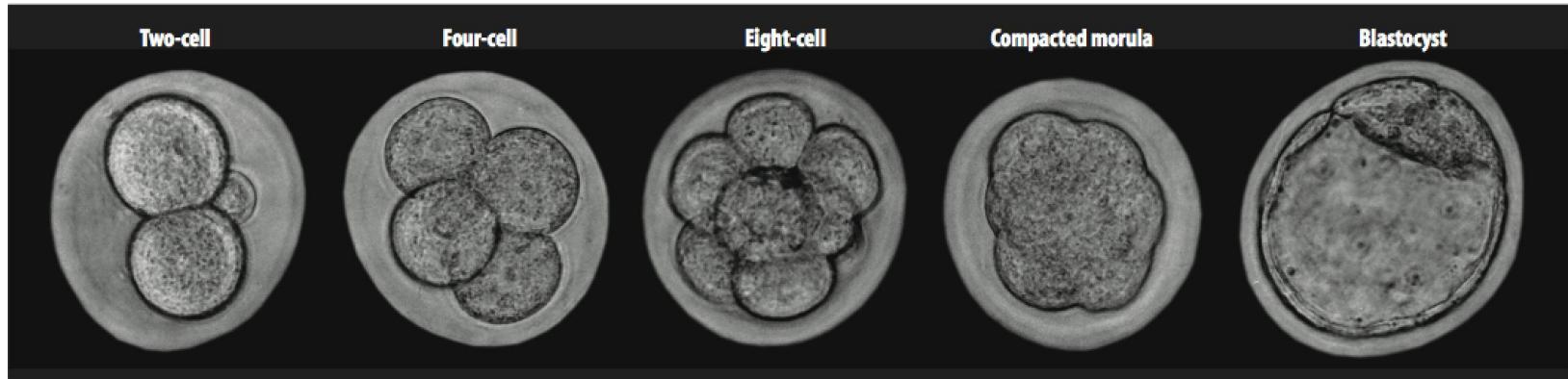
Life cycle of the mouse



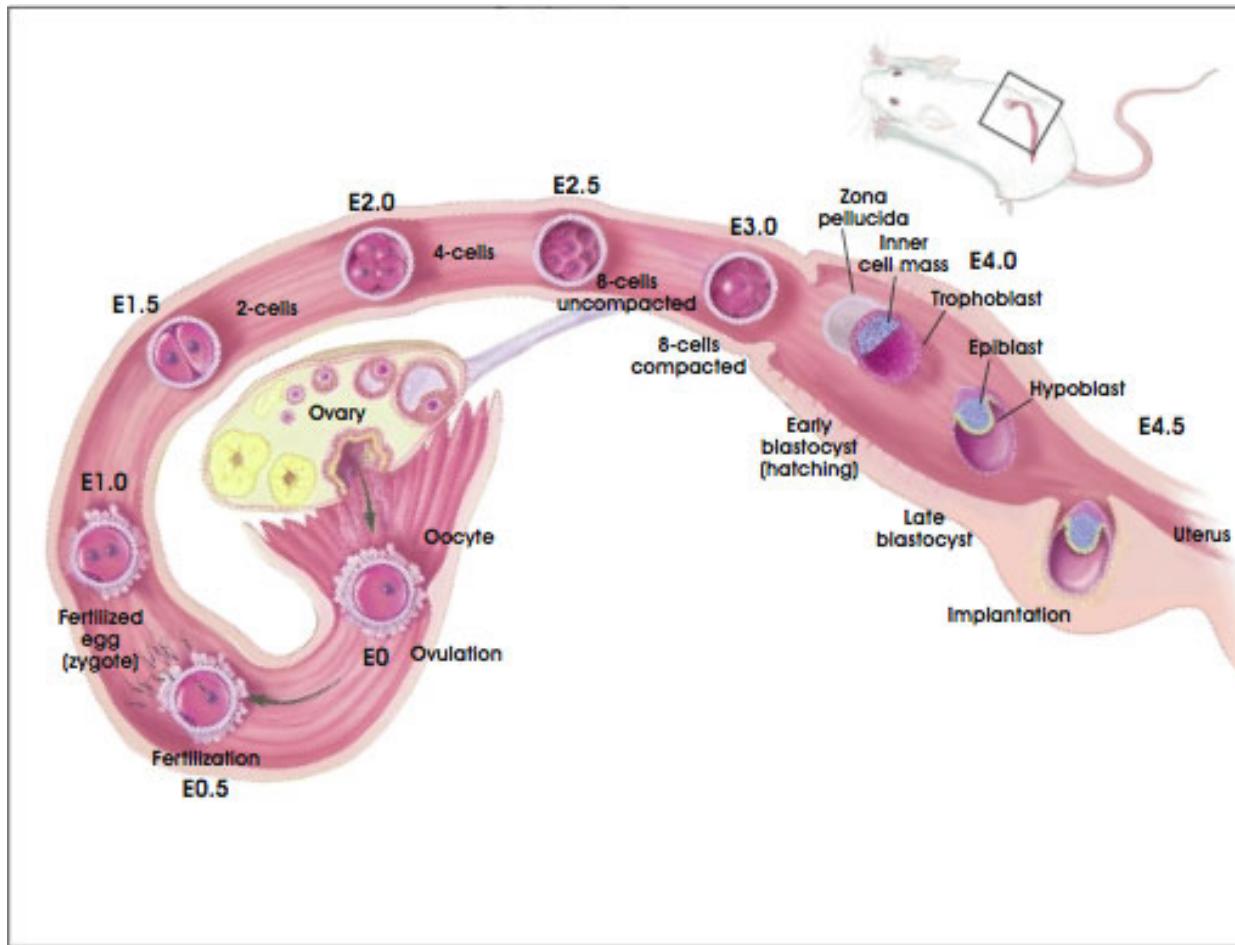
Features of mouse early embryogenesis I

- The egg is small and doesn't have yolk. The unfertilized egg is surrounded by a protective external coat, zona pelucida.
- Fertilization takes place in the oviduct.
- Meiosis of the egg is then completed and the second polar body forms.
- Early cleavages are very very slow compared with non mammal animals. 24 hpf, 1st. 44 hpf, 2nd. Then at about 12-hour intervals.

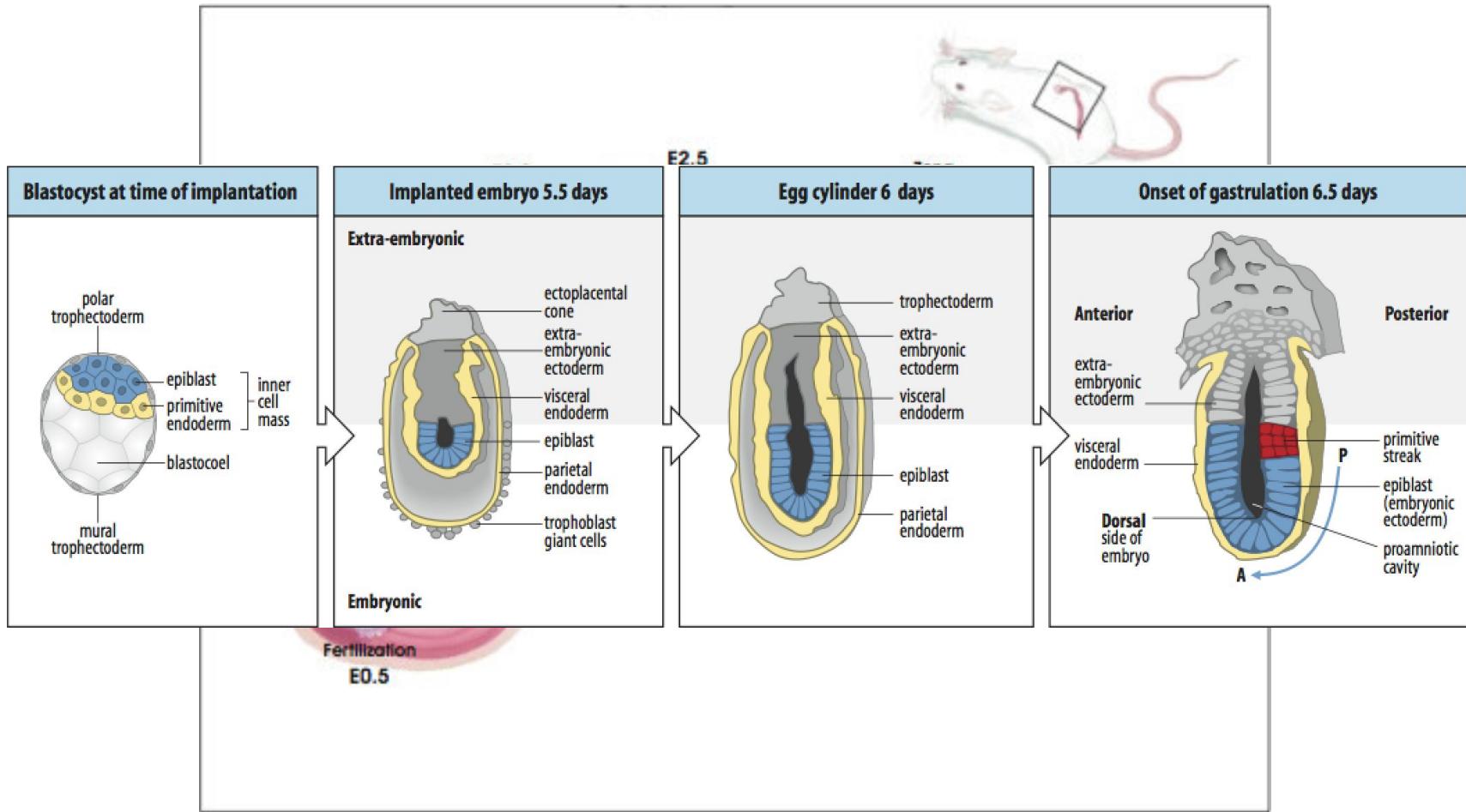
Cleavage in the mouse embryo



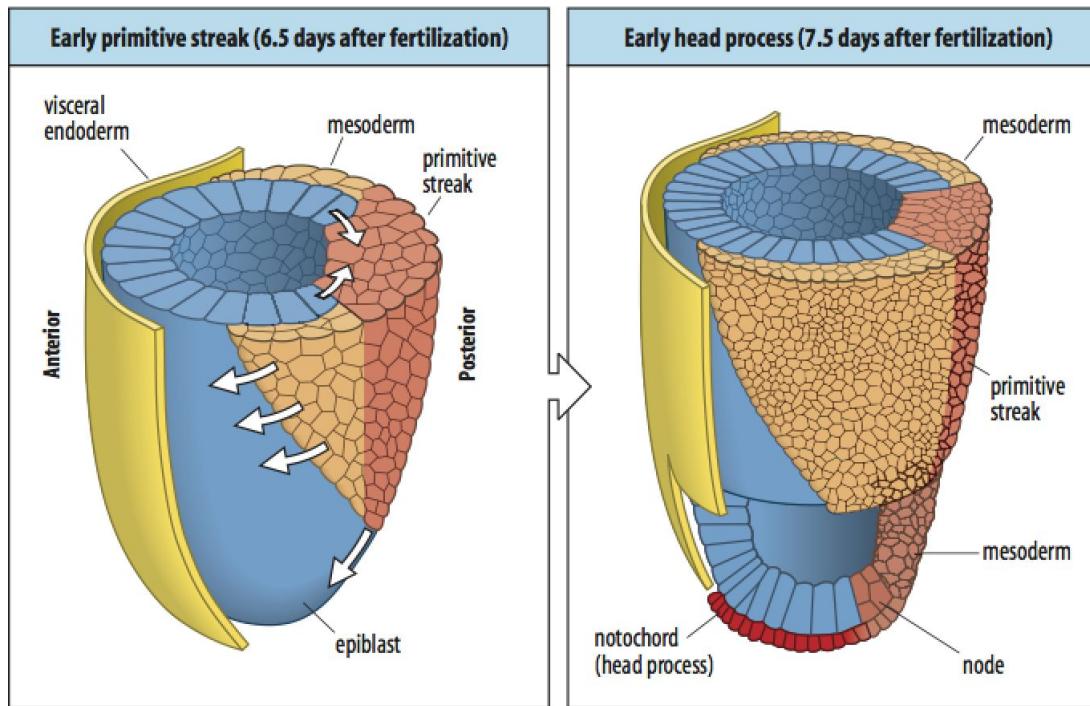
Early post-implantation development of the mouse embryo



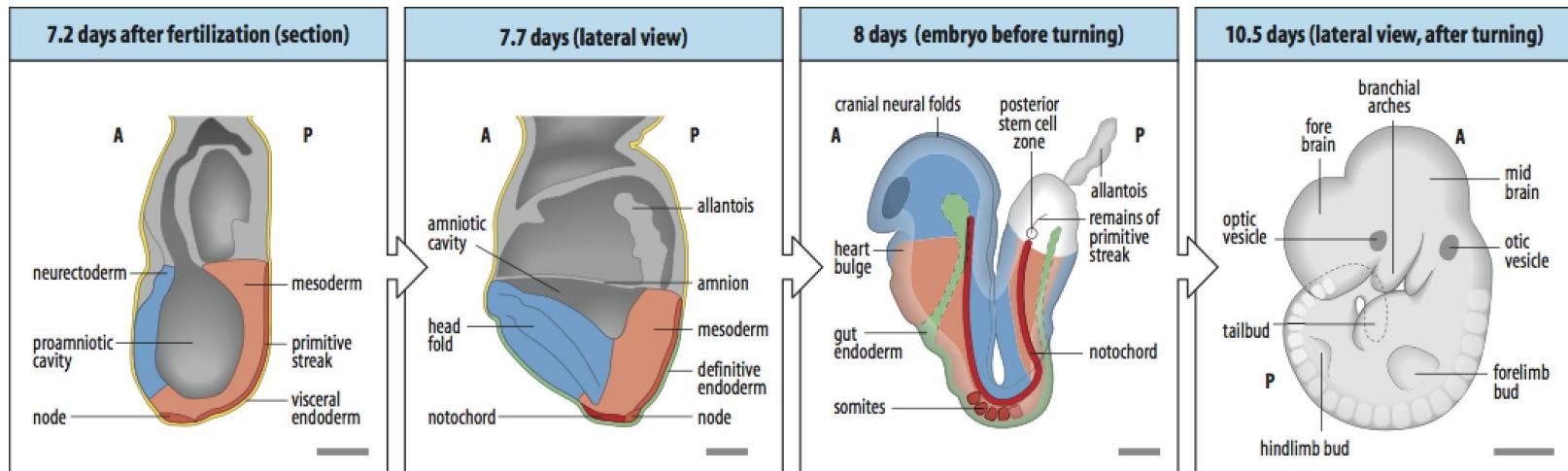
Early post-implantation development of the mouse embryo



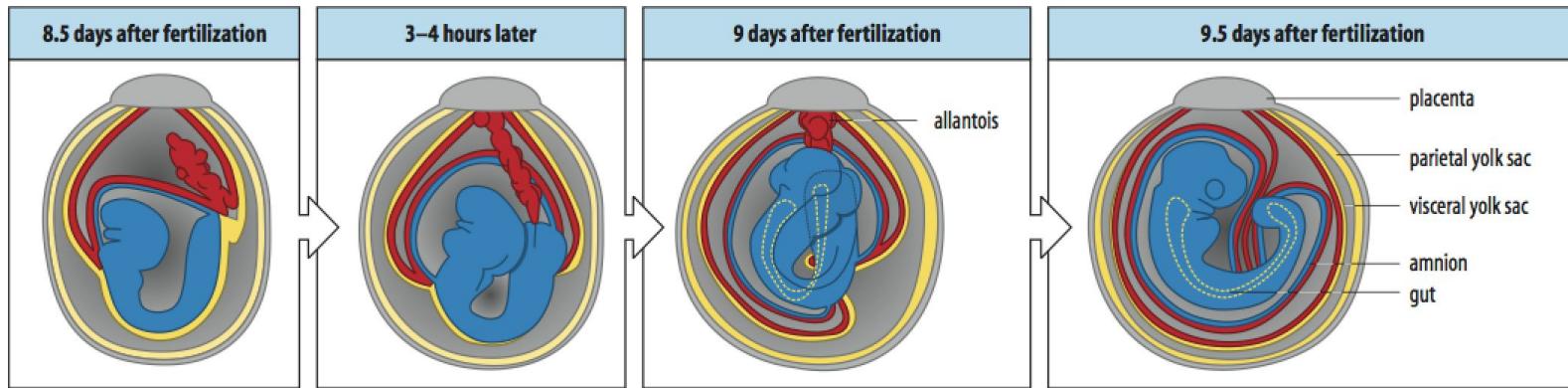
Gastrulation in the mouse embryo



Schematic views of the completion of gastrulation and neurulation

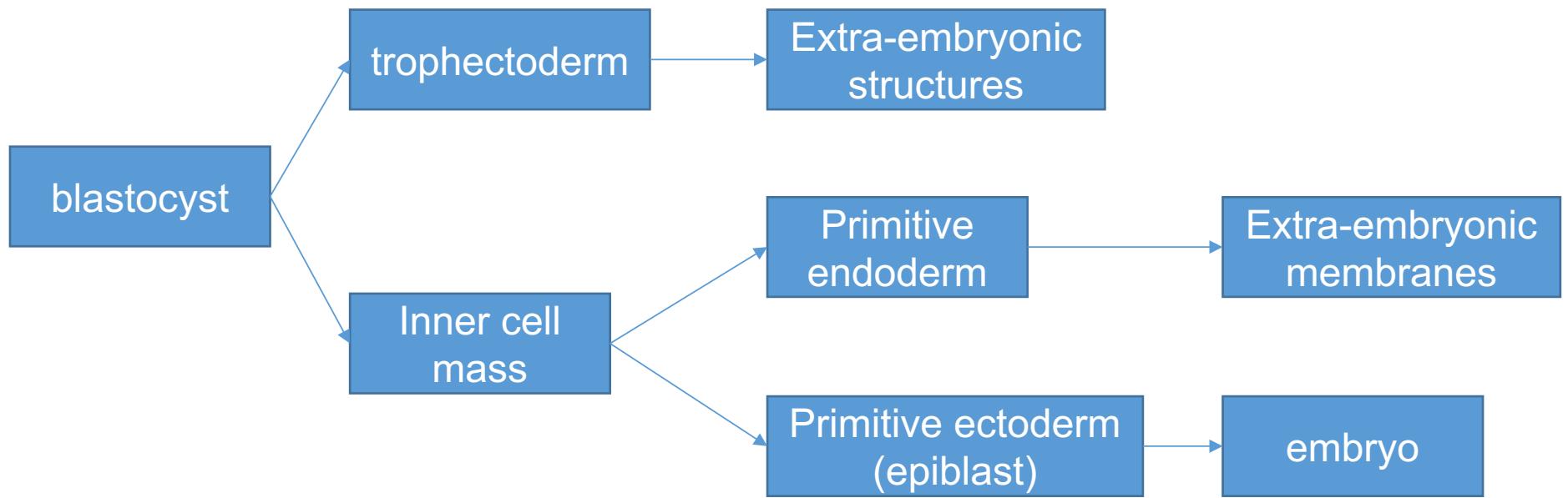


Turning in the mouse embryo



Features of mouse early embryogenesis II

- Blastocyst consists of trophectoderm and inner cell mass.
- The inner cell mass divides into two regions, the primitive endoderm and the primitive ectoderm (epiblast).
- The mural trophectoderm gives rise to primary trophoblast giant cell, in which DNA replicates without cell division.



Thanks!

Creation of a congenic strain

