東北大学脳科学 GCOE 共催セミナーのお知らせ

日　　時 ： 平成 20 年 1 月 15 日(火)午後 5 時から
(Tuesday, 15 January 2008, 17:00~)
場　　所 ： 加齢研大会議室
(Dai-kaigi-shitsu, IDAC Research Bldg.)
講　　師 ： 松永英治(Eiji Matsunaga)
所　　属 ： 理化学研究所脳科学総合研究センター・学術振興会
(RIKEN Brain Science Institute, Japan Society for the Promotion of Science.)
演　　題 ： Molecular basis of avian song system
講演言語 ： 日本語
担　　当 ： 仲村　春和(所属　分子神経研究分野・内線 8550)
Harukazu Nakamura (Molecular Neurobiology)

要　　旨 ：

Birds use various vocalizations for territory marking and courtship.

Among them, three families of birds (songbirds, parrots and hummingbirds) learn their vocalizations through imitation. Such an ability called 'vocal learning' is a fundamental basis of human verbal learning. Particularly, songbirds have been studied as good model animals for vocal learning. Based on numerous anatomical and physiological studies suggest so far that vocal learners have a neural network called 'song system' specialized for vocal learning and production in their brain. To explore the molecular basis of this system would help us to understand vocal behavior from the molecular to behavioral level, and through comparisons with other avian species without vocal learning ability, we can explore the evolution of vocal learning from a genetic perspective. In this seminar, I would like to introduce molecular study of the vocal system in songbirds and its evolution from an Evo-Devo perspective.

東北大学脳科学 GCOE 共催セミナーのお知らせ

日　　時 ： 平成 20 年 1 月 21 日(月)午後 4 時 30 分から
Monday, 21 January 2008, 16:30~
場　　所 ： 加齢研大会議室
Dai-kaigi-shitsu, IDAC Research Bldg.
講　　師 ： 太田訓正 (Kunimasa Ohta)
所　　属 ： 熊本大学 医学薬学研究部 (Kumamot Univ. Graduate School of Medicien.)
演　　題 ： Tsukushi による網膜幹細胞/前駆細胞の未分化性維持機構
(Tsukushi is a Frizzled4 ligand that, in competition with Wnt2b, regulates the proliferation of retinal stem/progenitor cells)
講演言語 ： 日本語
担　　当 ： 仲村 春和(所属 分子神経研究分野・内線 8550)
Harukazu Nakamura (Molecular Neurobiology)

要　　旨 ：

眼はほとんどの動物が持つ重要な感覚器官であり、外界からの80%以上の情報は眼を介して獲得される。神経網膜は、一度傷害を受けるとその機能を回復することはできないと考えられていたが、成体網膜での網膜幹細胞の発見により、細胞移植による機能再生が現実味を帯びてきている。神経網膜において、幹細胞/前駆細胞として機能しうる細胞は、毛様体、虹彩、網膜周辺部、網膜内で同定されており、その細胞増殖や分化の分子メカニズムは明らかになりつつある。しかしながら、幹細胞/前駆細胞が最終分裂を終えた後、これらの細胞がどのようにして未分化状態のままに維持されているかという問いには明確な答えは示されていない。

私達は、ニワトリ初期胚における発現パターンが土筆に似ていることから Tsukushi と名付けた分泌型プロテオグリカンが、動物種をこえて眼の幹細胞/前駆細胞が局在する毛様体辺縁部に発現していることを見出した。ニワトリ胚を用いた in vitro & in ovo の解析により、Tsukushi は Wnt2b による幹細胞/前駆細胞の増殖を阻害することが明らかになった。また、生化学的解析により、Tsukushi は細胞外領域において Wnt 受容体である Frizzled に直接結合し、Wnt の Frizzled への結合を阻害することが示された。さらに、Tsukushi KO マウスではコントロールのマウスと比べて、毛様体領域が拡張し、単離された Sphere の大きさやその数が増加していた。以上の結果は、Tsukushi が Wnt シグナルを阻害することにより、網膜幹細胞/前駆細胞を未分化性に維持するニッチ分子として機能することを示唆するものである。

Wnt signalling orchestrates multiple aspects of central nervous system development, including cell proliferation and cell fate choices. In chick retina, Wnt2b is expressed in both the surface ectoderm and the retinal pigmented epithelium at optic cup stage. At later stage, Wnt2b is expressed in the marginal-most tip of the embryonic chick retina. Using a clonal assay in retinal re-aggregation cultures, along with overexpression studies, it was proposed that Wnt2b plays a role in the proliferation of retinal progenitor cells without cell differentiation (Kubo et al., 2005).

We have identified a BMP antagonist, Tsukushi (TSK), which is a soluble molecule containing 12 leucine-rich repeats and belongs to the Small Leucine-Rich Proteoglycan family (Ohta et al., 2004). TSK is expressed in the primitive streak and Hensen's node during chick gastrulation and involved in their formation (Ohta et al., 2004; Ohta et al., 2006). TSK is also involved in the neural crest specification of Xenopus embryo by regulating BMP and Delta-1 activities at the boundary between the neural and the non-neural ectoderm (Kuriyama et al., 2006). Further, TSK contributes to germ layer formation and patterning in Xenopus development by modulating Xnr2, FGF, and BMP signalling (Morris et al., 2007).

When Wnt2b was over-expressed into chick optic vesicle at stage 10, Wnt2b induced prolonged proliferation of retinal progenitor cells in vitro. However, when Wnt2b was co-over-expressed with TSK, which is also expressed in the marginal-most tip of the chick retina, the proliferative activity of Wnt2b was almost inhibited. Biochemical analyses showed that TSK functions as a Wnt signaling inhibitor by direct binding to Frizzled4 at the extracellular region. In the mouse retina, TSK is expressed in the ciliary body (CB) in which retinal stem/progenitor cells are located, and targeted disruption of TSK in mouse resulted in the expansion of the CB and an increase in the number of retinal spheres. Using gain- and loss-of function studies, we uncover a new crucial role for TSK in maintaining the growth and undifferentiated properties of retinal stem/progenitor cells as a niche molecule.

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日　　時 ： 平成 20 年　1 月　22 日(火)午後　4 時～
場　　所 ： 加齢研大会議室
講　　師 ： Daniel H Turnbull
所　　属 ： Departments of Radiology (Skirball) and Pathology, New York City University
予定演題 ： Ultrasound and MR Micro-imaging of Mouse Brain Development

講　　師 ： Alexandra Joyner
所　　属 ： Memorial Sloan-Kettering Cancer Center
予定演題 ： Patterning the cerebellum in 3
dimensions ： from lobules and molecular stripes to circuits

The most noticeable morphological feature of the cerebellum is its folded appearance, whereby fissures separate its anteriorposterior extent into lobules. Each lobule is molecularly coded along the mediallateral axis by parasagittal stripes of gene expression in the Purkinje cells (PC). Additionally, within each lobule distinct combinations of afferents terminate and supply the cerebellum with synchronized sensory and motor information. Strikingly, afferent terminal fields are organized into parasagittal domains, and this pattern bears a close relationship to PC molecular coding. Thus, cerebellum three-dimensional complexity is reflected in a basic coordinate system that can be broken down into morphology and molecular coding. We are studying the genetic and cellular events that regulate formation of the coordinate system and whether the circuitry map is dependent on patterning of the lobules and parasaggital stripes. We have found that a key event in initiation of foliation is the acquisition of a distinct cytoarchitecture at the base of each fissure that we term “anchoring centers”, and that the precise timing of the appearance of anchoring centers at the prospective base of each fissure and the subsequent coordinated function of granule cells and Bergmann glia dictates the shape of the folia. Our preliminary analysis of an allelic series of Engrailed1 (En1) and/or En2 homeobox mutants indicates that En1/2 regulate the continuum of foliation patterns from the medial vermis to the hemispheres by controlling a morphogenetic clock that determines when each of the anchoring centers forms along the anterior-posterior axis. In addition, we find that En1/2 regulate the pattern of the molecular code in the vermis independent of their function in patterning foliation. Furthermore, the topography of lumbar spinocerebellar mossy fiber terminal fields is altered in En mutants, and the alterations correlate with changes in parasagittal molecular domains and not lobules.