PhD studentships at the Liu Lab, University of Oxford (starting in Oct 2015)

Metabolic cell biology

CTP synthase, Cytoophidia, Cancer and CRISPR

Project Supervisor	Dr Ji-Long Liu (**jilong.liu@dpag.ox.ac.uk**)
MRC Funding	**Available to students resident in the UK and EU ONLY (Deadline Monday 3rd November 2014) *http://www.findaphd.com (search "CTP")***
Other Funding	**Available to both international and home students (Deadline Friday 15th January 2015) *http://www.dpag.ox.ac.uk/study/for-graduates***

Our lab has discovered that CTP synthase is compartmentalized in a novel organelle, the cytoophidium (1-6). Moreover, cytoophidia are detectable in bacteria, yeast and mammals (review see 7). Compartmentation is essential for the localization of biological processes within a cell. CTP synthase has been an attractive target for developing agents against cancer, virus and parasites. The high conservation and widespread distribution of the cytoophidium among diverse organisms and cell types indicates that this novel compartment contributes to fundamental cellular processes.

CTP synthase has been found upregulated in many types of cancer cells. CTP synthase has been an attractive target for developing agents against cancer, virus and parasites. Our long-term goal is to understand mechanisms of CTP compartmentalization within a cell. We will investigate how CTP synthase is assembled into the cytoophidium and how the cytoophidium is linked to cancer biology.

More recently, our lab has described a method for efficiently creating mutations in chosen *Drosophila* genes within a month based on the CRISPR/Cas9 system from bacteria (8). We will continue to develop and apply this cutting-edge genome engineering technology to generate multiple mutants for studying the biology of cytoophidia.

This project will address one of the following questions depending on the student's interest.

- To study the role of cytoophidia in cancer biology.
- To characterize the ultrastructure and dynamics of cytoophidia.
- To determine the principal functions of cytoophidia.
- To search for factors regulating the biogenesis of cytoophidia.
- To apply CRISPR genome engineering technology to generate mutants to study cytoophidia.

Techniques and training will include CRISPR, RNAi screening, RNA-Seq, laser-scanning confocal microscopy, single-cell mutagenesis, metabolomics profiling, cellular and molecular biology, live imaging, developmental neuroscience and *Drosophila* and yeast genetics.

References

1. Liu JL. (2010). Intracellular compartmentation of CTP synthase in *Drosophila*. *Journal of Genetics and Genomics* 37(5):281-96.
2. Chen K*, Zhang J*, Tastan ÖY*, Deussen ZA, Siswick MY and Liu JL. (2011). Glutamine analogs promote cytoophidium assembly in human and *Drosophila* cells. *Journal of Genetics and Genomics 38(9):391-402*. (cover story)
3. Azzam G and Liu JL. (2013). Only one isoform of *Drosophila melanogaster* CTP synthase forms the cytoophidium. *PLOS Genetics* 9(2): e1003256.
4. Gou KM*, Chang CC*, Shen QJ, Sung LY** and Liu JL**. (2014). CTP synthase forms cytoophidia in the cytoplasm and nucleus. Experimental Cell Research 323(1):242-253.
5. Aughey G, Grice S, Shen QJ et al. (2014). Nucleotide synthesis is regulated by cytoophidium formation during neurodevelopment and adaptive metabolism. *Biology Open* [Epub 17 Oct 2014]
6. Zhang J, Hulme L and Liu JL. (2014). Asymmetric inheritance of cytoophidia in *Schizosaccharomyces pombe*. *Biology Open* (in press).
7. Liu JL. (2011). The enigmatic cytoophidium: compartmentation of CTP synthase via filament formation. *BioEssays* 33(3):159-64. (cover story)
8. Bassett AR, Tibbit C, Ponting CP and Liu JL. (2013). Highly efficient targeted mutagenesis of *Drosophila* with the CRISPR/Cas9 system. *Cell Reports* 4(1):220-8.

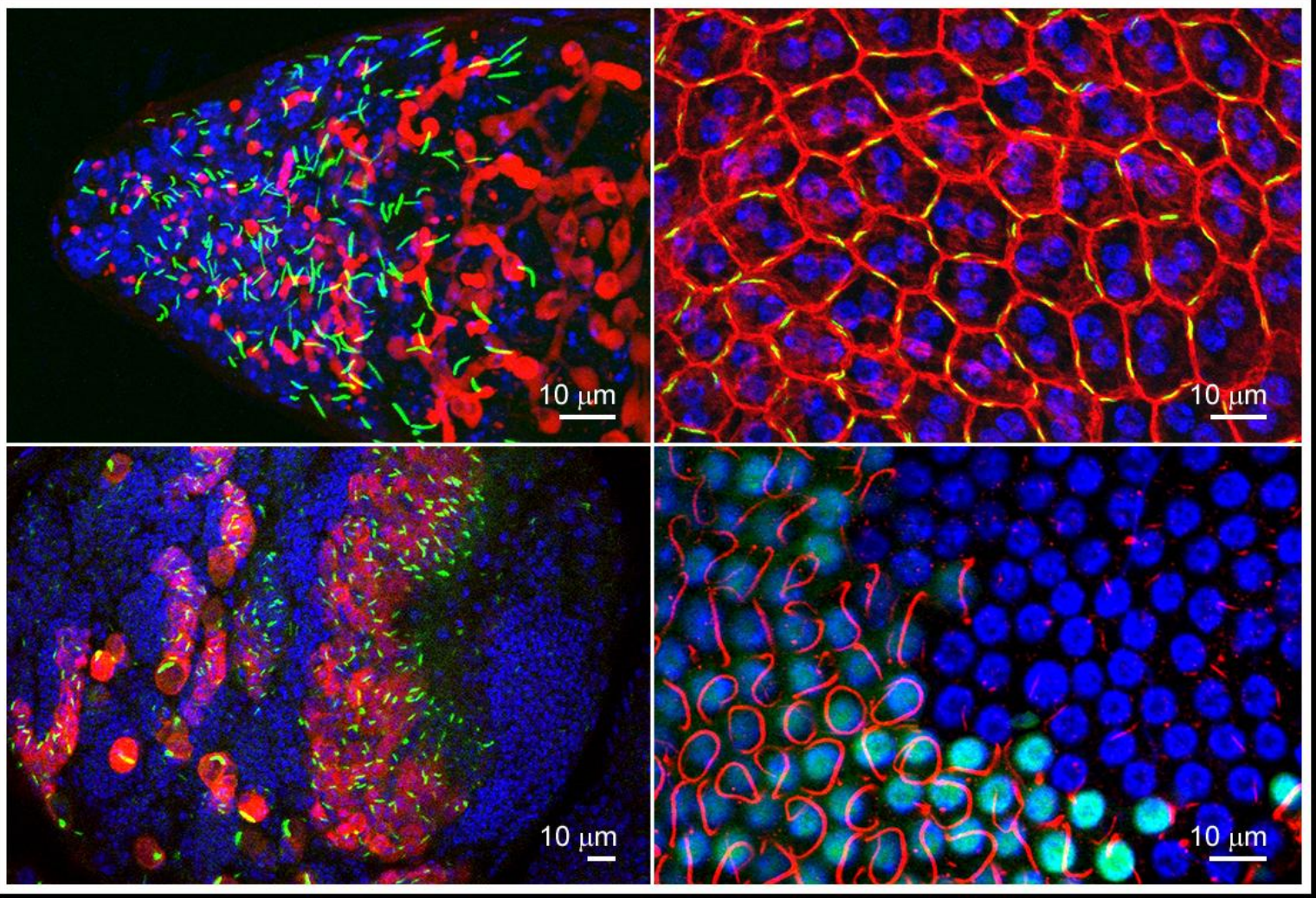
For more information please visit the Liu Lab websites

http://groups.mrcfgu.ox.ac.uk/liu-group/contact-us

http://www.dpag.ox.ac.uk/research/liu-group

Cell PICTURE SHOW

Cell Curiosities - Metabolic Serpents



Metabolic Serpents

Ji-Long Liu, Oxford University, UK

Cytoophidia (Greek for "cell snakes") are evolutionarily conserved, cytoplasmic structures composed of the enzyme CTP synthase. Although their exact function is unknown, Liu and others posit that the self-association of the enzyme into filamentous structures facilitates the regulation of key cellular metabolism pathways.

Image: Cytoophidia light up as green filaments in the *Drosophila* testis (upper-left), brain (lower-left), and accessory gland (upper-right) with a fluorescent fusion to CTP synthase (Chen, K., et al. [2011]. J. Genet. Genomics 38, 391–402). Exceptionally long, red filaments appear in follicle cells with green nuclei in the *Drosophila* ovary (lower-right) when a specific CTP synthase isoform is expressed inside of them (Azzam, G., and Liu, J.L. [2013]. PLoS Genet. 9, e1003256).

Please get in touch with Dr Ji-Long Liu (jilong.liu@dpag.ox.ac.uk)

For more information please visit the Liu Lab websites
http://groups.mrcfgu.ox.ac.uk/liu-group/contact-us
http://www.dpag.ox.ac.uk/research/liu-group

Liu Lab MRC FGU, Oxford

MRC Functional Genomics Unit

University of Oxford