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LES SÉMINAIRES DE L'INMG

Stochastic gene expression and nuclear architecture in fly eyes and human retinal organoids

par

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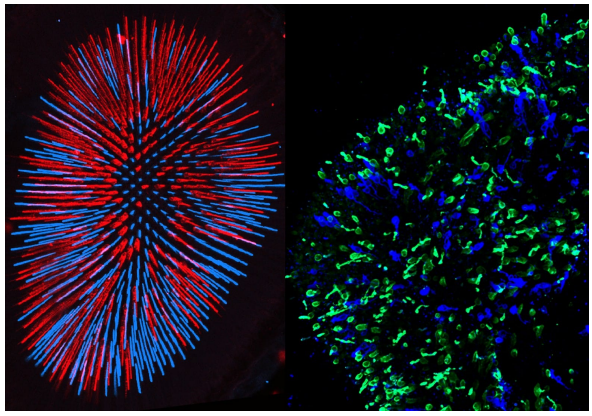
Abstract



A central challenge in developmental neurobiology is to understand how the myriad types of neurons in the human nervous system are generated. Stochastic gene expression mechanisms are crucial to differentiate neuronal subtypes and expand function. During stochastic fate specification, individual neurons randomly choose between different fates, resulting in unique patterns but consistent proportions of cell types among genetically identical organisms.

My lab studies the stochastic mechanisms that specify the color-detecting photoreceptors in the fly and human retina. Fruit flies have a well-characterized retina and an abundance of genetic tools that enable molecular analyses of gene regulatory mechanisms. To overcome the challenges associated with human studies, we have developed a human retinal organoid system that recapitulates retinal development and photoreceptor specification. With these systems, we are interrogating how DNA elements, trans factors, and chromatin architecture control random on/off gene expression. Our molecular approaches are complemented by quantitative genetics to determine how natural variation in the genome impacts gene expression and photoreceptor specification. Finally, we conduct behavioral and functional assays to measure differences in color perception when photoreceptor fates are altered. By studying highly divergent organisms from multiple angles, we aim to define the unifying principles underlying stochastic fate specification during nervous system development.

Selected Publications

Anderson, C., Reiss, I., Zhou, C., Cho, A., Siddiqi, H., Morman, B., Aviles, C.M., Deford, P., Bergland, A., Roberts, E., Taylor, J., Vasiliauskas, D., and **Johnston, R.J., Jr.** (2017)
Natural variation in binding site affinity controls stochastic gene expression and color perception.
***eLife**, 6,* e29593.

Yan, J., Anderson, C., Viets, K., Tran, S., Goldberg, G., Small, S., and **Johnston, R.J., Jr.** (2017)
Regulatory logic driving stable levels of *defective proventriculus* expression during terminal photoreceptor specification in flies.
Development, *144*, 844-855.

Johnston, R.J., Jr., and Desplan, C. (2014)
Interchromosomal communication coordinates intrinsically stochastic expression between alleles.
Science, *343*, 661-665.

Thanawala, S.U., Rister, J., Goldberg, G.W., Zuskov, A., Olesnicky, E.C., Flowers, J.M., Jukam, D., Purugganan, M.D., Gavis, E.R., Desplan, C., and **Johnston, R.J., Jr.** (2013)
Regional modulation of a stochastically expressed factor determines photoreceptor subtypes in the *Drosophila* retina.
Dev Cell, *25*, 93-105.

Vasiliauskas, D., Mazzoni, E.O, Sprecher, S.G., Brodetskiy, K., **Johnston R.J., Jr.**, Lidder, P., Vogt, N., Celik, A., and Desplan, C. (2011)
Feedback from rhodopsin controls *rhodopsin* exclusion in *Drosophila* photoreceptors.
Nature, *479*, 108-112.