Research

RNA in disease and translational technologies

The Aw lab is interested in understanding roles for RNA, in particular microRNA (miRNA), in neurodegeneration and movement disorders, and exploiting RNA biology to develop translational technologies based on novel functional RNA molecules, for disease diagnosis and therapeutics.

To do this, we take a cross-disciplinary approach, combining genetics, biochemistry and chemistry, behavioural assays, high-speed imaging and computational analysis, collaborating closely with computer scientists, chemists and engineers.

1. RNA in disease

MiRNA, a class of short, non-coding RNA involved in gene regulation, carry out important functions in most biological systems and are implicated in many diseases. We carry out functional screens of miRNA mutants, and molecular and biochemical characterization of conserved miRNA regulatory pathways, to understanding how defects in miRNA biology can lead to diseases like neurodegeneration, tremor and movement disorder.

Aw, S. *#, Lim, KH, Tang, XM, Cohen, SM.***** (2017) *A glio-protective role of mir-263a by tuning sensitivity to glutamate*. **Cell Reports** *19(9): 1783–93*

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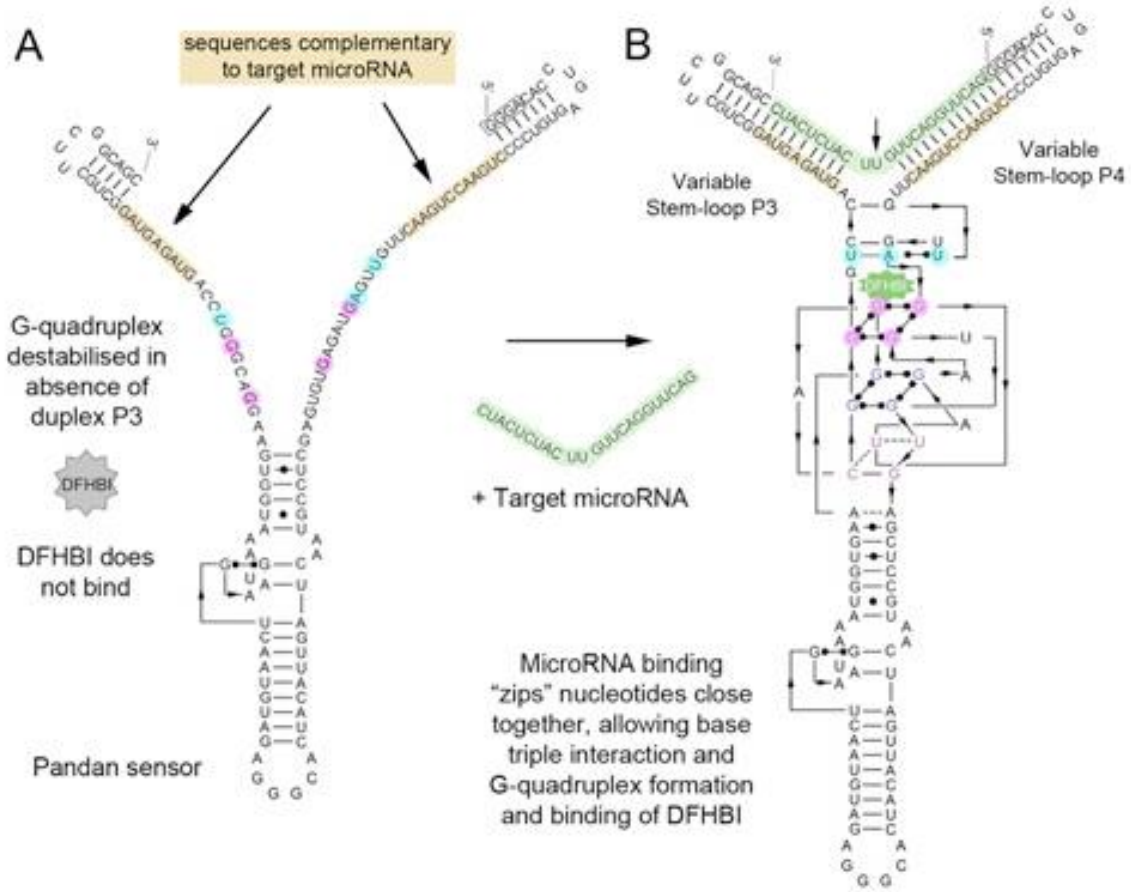
2. RNA technologies for diagnostics and therapeutics



Besides functioning in gene regulation and disease pathways, miRNA also have emerging roles as clinical biomarkers useful for disease diagnosis. Innovations in techniques to sense and quantify miRNAs may aid research into novel aspects of miRNA biology and contribute to the development of RNA-based diagnostics. By introducing an additional stem loop into the fluorescent RNA Spinach and altering its 3' and 5' ends, we generated a new RNA, Pandan, that functions as the basis for a miRNA sensor (Aw et. al., NAR 2016, PCT/SG2017/050086 2017).

While Pandan exhibits large fluorescent fold changes and is specific for its target miRNA, it was not sensitive enough for detection of miRNA at endogenous levels, as the RNA is not

amplified (as is normally carried out in RT-qPCR). Hence, we developed a second RNA molecule, a ribozyme able to sense and amplify RNA signals (PCT/SG2020/050226 2020).

We are further developing these two molecules for clinical diagnostics for diseases in which RNA serve as useful biomarkers, including COVID-19. We also aim to genetically encode these RNA sensors *in vivo*, for drug screening and therapeutic applications.

References:

Aw, S.*#, Tang, XM., Teo, YN*****, Cohen, SM. (2016) *A conformation-induced fluorescence method for microRNA detection*. ***Corresponding #Lead contact**

Nucleic Acids Research 44 (10): e92, *doi: 10.1093/nar/gkw108*

Mandy Lim, Koh Chong Hui and Sherry Aw (2020) *A ribozyme comprising a target-binding domain.* **PCT patent application** 2020 - PCT/SG2020/050226

Sherry Aw, Melissa Tang, Teo Yin Nah and Stephen Cohen. *A simple one-step real-time molecular sensor for microRNA detection* **PCT patent application** 2018 (US and Singapore) - PCT/SG2017/050086; **Singapore provisional patent** 2014 #10201601384T - IMC/P/08599/01/SG

3. Machine learning for study of movement disorder

Movement defects often accompany neurodegenerative diseases, and are used as a basis for diagnosis. To better characterise these defects, we developed a fully automated machine learning-based tracking and gait analysis system for fly disease models. We are using our automated tracking system to link cellular dysfunction to behavioral outputs, in order to understand the genes and circuits that underlie disease, including miRNA.

Reference:

Shuang Wu, Kah Junn Tan, Lakshmi Narasimhan Govindarajan, James Charles Stewart, Lin Gu, Joses Wei Hao Ho, Malvika Katarya, Boon Hui Wong, Eng King Tan, Daiqin Li, Adam Claridge-Chang, Camilo Libedinsky, Li Cheng* and **Sherry Shiying Aw*#** (2019) *Fully*

automated leg tracking of Drosophila neurodegeneration models reveals distinct conserved movement signatures.

PLOS Biology*17(6):e3000346.* ****Corresponding authors #Lead contact***