Yale Center for Molecular Discovery

Spring 2015 Newsletter

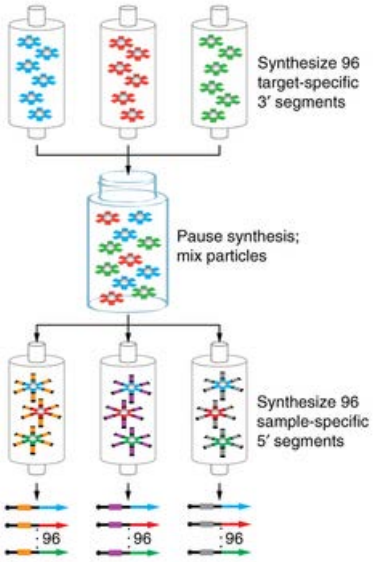
Contents

Featured Project

Patel Lab: High-throughput RNA profiling via up-front sample parallelization

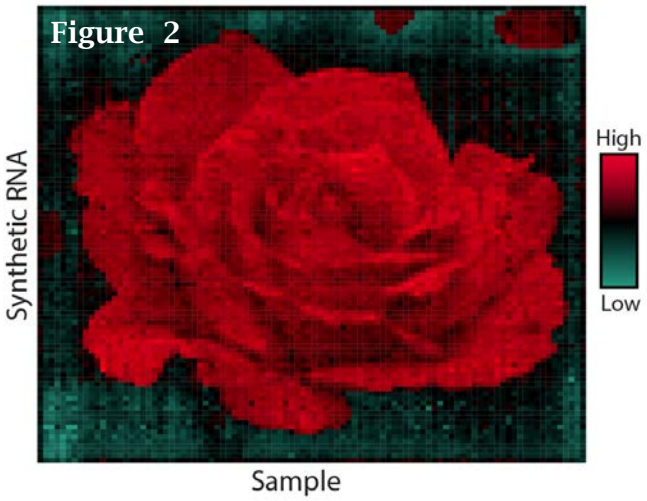
Quantitative gene expression studies have the power to characterize complex cellular physiology and diseases. In a new method from the Patel lab, modular, early-tagged amplification (META) RNA profiling has enabled highly parallel analysis of predetermined RNAs across multiple samples in a rapid and cost-effective approach.

Figure 1



In the first step of processing, each sample is individually tagged during reverse transcription with an oligonucleotide that has been synthesized in a modular fashion (**Figure 1**, left). The sample capture primers have a target-specific 3' segment corresponding to an mRNA or miRNA of interest and 5' sample marker segment. After the reverse transcription step, all of the tagged cDNAs are pooled, purified, and arrayed according to the number of targets to be measured. PCR that utilizes the target-specific portion of the tag follows with one target per well. This feature of pooled amplification achieves cross-sample quantitative accuracy as well as removes the difficulties of sampling genes with large differences in transcript abundance. In the last step, massively parallel sequencing of the PCR products is followed by counting the sample-specific tags associated with each mRNA or miRNA target.

Figure 2



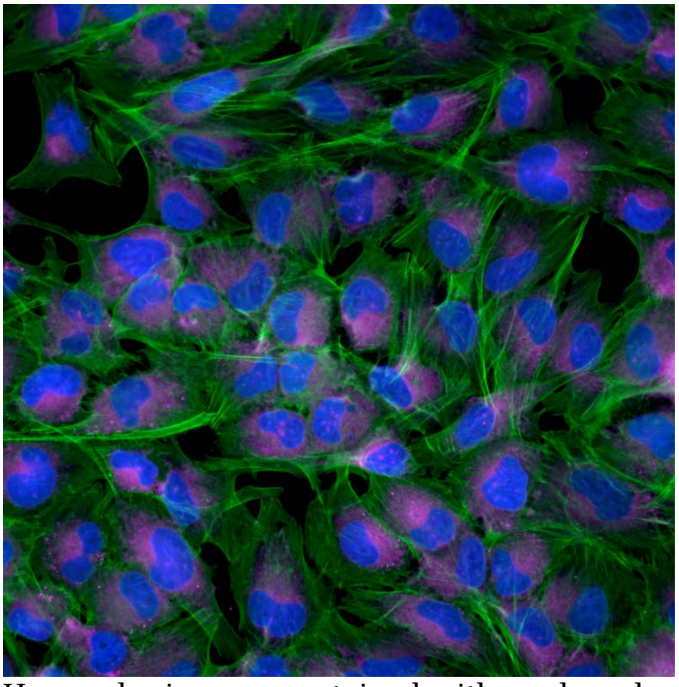
In a beautiful proof of concept study, the pixels of a digital photo of a rose were numerically converted to microliters of 96 individual RNAs (pixel row) and robotically dispensed at YCMD to 96 sample tubes (pixel column). The resulting heat map (**Figure 2**, above) was generated from the results of quantitative sequencing. For more details, please see the full reference here.

Short-term Pilot Projects

Congratulations to the 8 PIs awarded short-term pilots of up to 50 hours of fully-subsidized Center use for assay development, imaging/analysis algorithm development, and up to 15 small molecule or siRNA library plates. Our goal is high quality preliminary data by May 15, 2015 for PI-initiated grant applications for the June 5, 2015 NIH R01 submission deadline. Please let us know what you think about this initiative.

New Technologies

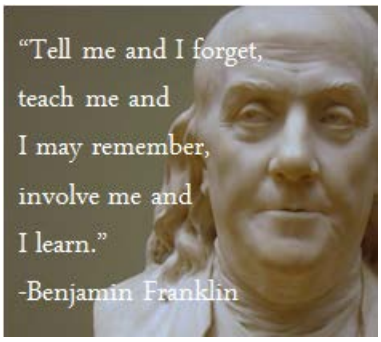
Cell organelle staining: The overlay image below of cell organelles was taken on YCMD's own GE IN Cell 2200 with a 40X objective lens.



Human brain cancer, stained with nuclear dye Hoechst, reticulum dye Concavalin A, and cytoskeleton dye Phalloidin.

2015 Internships

YCMD is continuing to sponsor its ten-week summer undergraduate research paid internships for students entering their sophomore, junior or senior years and who are interested in exploring a professional career as a research scientist with hands-on experience. We seek talented students who crave learning new skills and contributing to a research pipeline that serves Yale University. Interns will work with a number of our research staff and will take on real world projects that will help us grow. Our ideal candidate is someone who is strategic and responsible with the research they pursue.



This year's exciting projects are:

1. Investigation of cancer cell spheroid growth and analysis
2. Protocol development for machine learning for phenotypic cellular analysis
3. Chemical biology: screening for enzyme inhibitors using mass spectrometry

Follow this link to see more information.

Wishlist

Is there a high throughput technology you wish you had access to that would facilitate your research? Please let us know.

We continually seek information to communicate the value of YCMD efforts to faculty.
Acknowledgement on papers and tracking publications resulting from work performed at the Center is critical to our success.
Please keep these updates flowing.

Recent Center Publications

Farley KI, **Surotseva Y**, **Merkel J**, Baserga SJ. Determinants of mammalian nucleolar architecture. Chromosoma. 2015 Feb 12. doi: 10.1007/S00412-015-0507-z

Kinch MS, **Umlauf S**, **Plummer M**. An Analysis of FDA-approved drugs for metabolic diseases. Drug Discov Today. 2015 February 11. doi: 10.1016/j.drudis.2015.02.002

Patridge E, **Gareiss P**, Kinch MS, **Hoyer D**. An analysis of FDA-approved drugs: natural products and their derivatives. Drug Discov Today. 2015 Jan 21. doi: 10.1016/j.drudis.2015.01.009

Kinch MS, **Hoyer D**, Patridge E, **Plummer M**. Target selection for FDA-approved medicines. Drug Discov Today. 2014 Nov 11. doi: 10.1016/j.drudis.2014.11.001

YCMD Web Links

See the resources YCMD has to support your research:

Screening Collections Instrumentation Software
Feedback or questions