Bioconductor Software Packages for LISH-seq Probe Design and Data Analysis

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APTRC

"Activitives to promote technology research collaborations (APTRC) for cancer research"

A collaboration between two grants, one from each of
ICTR - "Informatics Technology for Cancer Research"
IMAT - "Innovative Molecular Analysis Technologies"

In our case
ICTR: U24 (PI: Morgan), focus: Bioconductor
[Hansen has a sub-award on this grant]
IMAT: R21 (PI: Larman), focus: LISH

LISH - "Ligation *in-situ* hybridization" is a method for measuring RNA expression (later).

Key focus of our admin support: to develop the informatics tools necessary to take LISH from proof-of-concept to a commodity assay.

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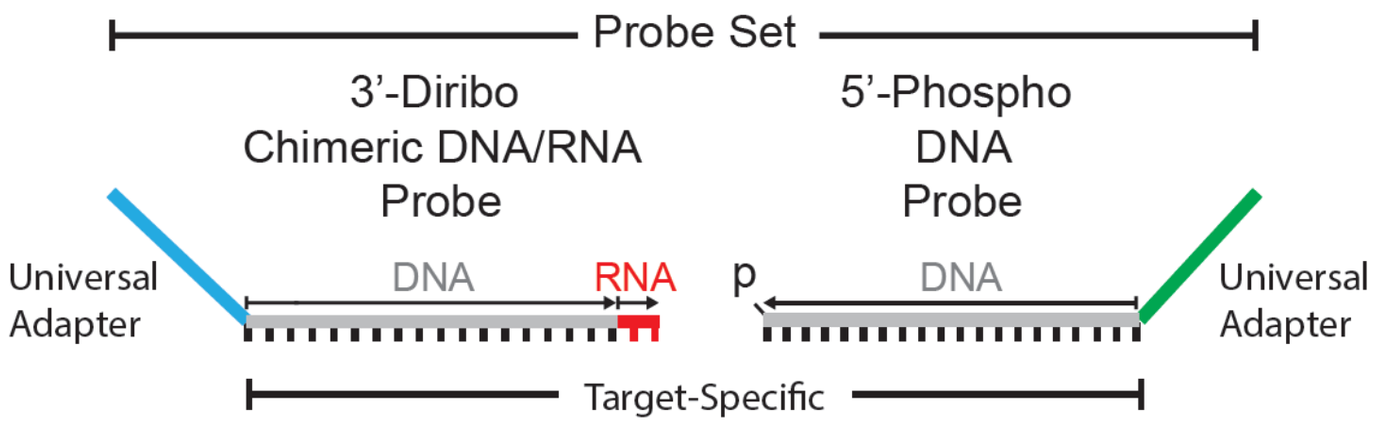
Multiplexed analysis of fixed tissue RNA using Ligation *in situ* Hybridization

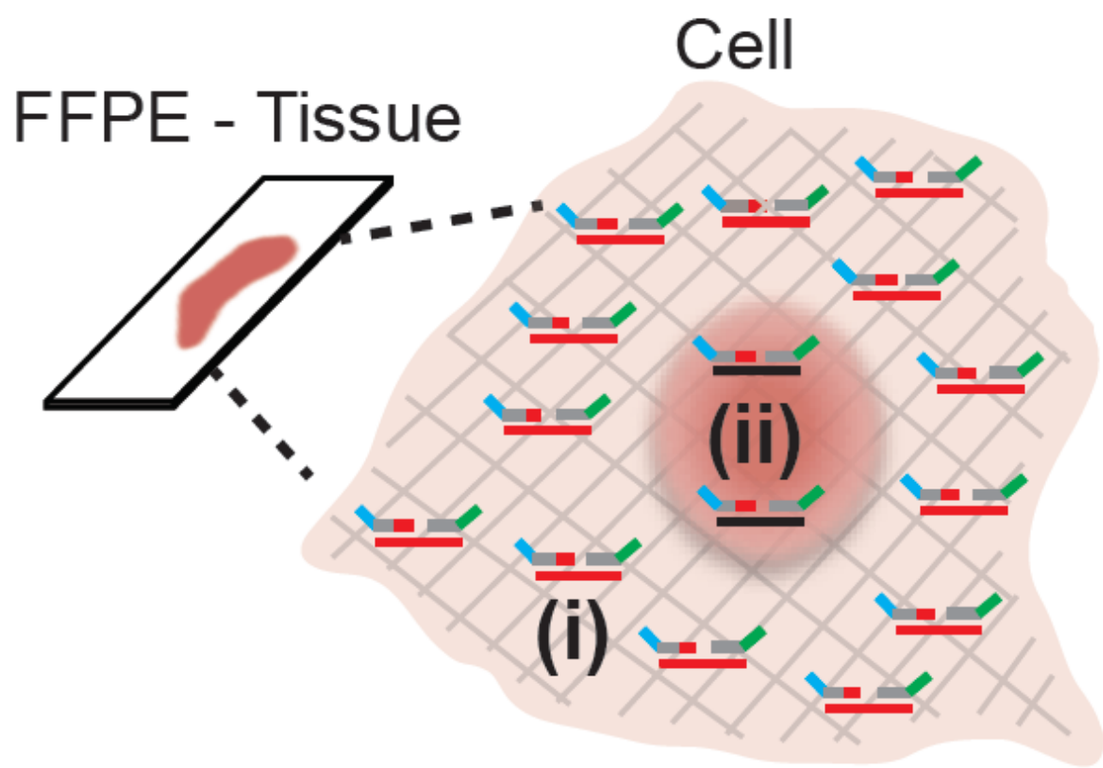
Joel J. Credle[1], Christopher Y. Itoh[1], Tiezheng Yuan[1], Rajni Sharma[1], Erick R. Scott[2], Rachael E. Workman[3], Yunfan Fan[3], Franck Housseau[4], Nicolas J. Llosa[4], W. Robert. Bell[5], Heather Miller[5], Sean X. Zhang[5,6], Winston Timp[3] and H. Benjamin Larman[1,*]

LISH - Ligation *in-situ* hybridization

Developed by Ben Larman's lab at JHU.



Two probes
DNA/RNA mix



Advantages of LISH

- Does not require isolation or RT of fixed RNA
- Higher per-molecule sensitivity than RT-qPCR/RNA-seq
- Compatible with a variety of routine strains
- Can be performed sequentially on the same section.
- Sample multiplexing can dramatically reduce cost
- No proprietary reagents or specialized resources.

Ongoing studies

- Transcriptome-wide LISH
- Tumor microenvironment using tissue microarrays.
- Adapting LISH to multiplexed fluorescent imaging in situ.

Informatics

To help LISH become a widely used method we need to address the following

Aim 1: Develop data-driven LISH probe design software.

Aim 2: Develop an analytical software package for LISH data sets.

To accomplish these aims we planning and doing a series of informative experiments which will give us the necessary data to develop methods and software. We have expertise in both in the Bioconductor team.