The BioPhenics Platform

High Content Screening for Large Scale Functional Biology, Drug Discovery & Target Validation

Platform's mission is to work with research teams as a partner for both basic and applied research projects

Basic aim:

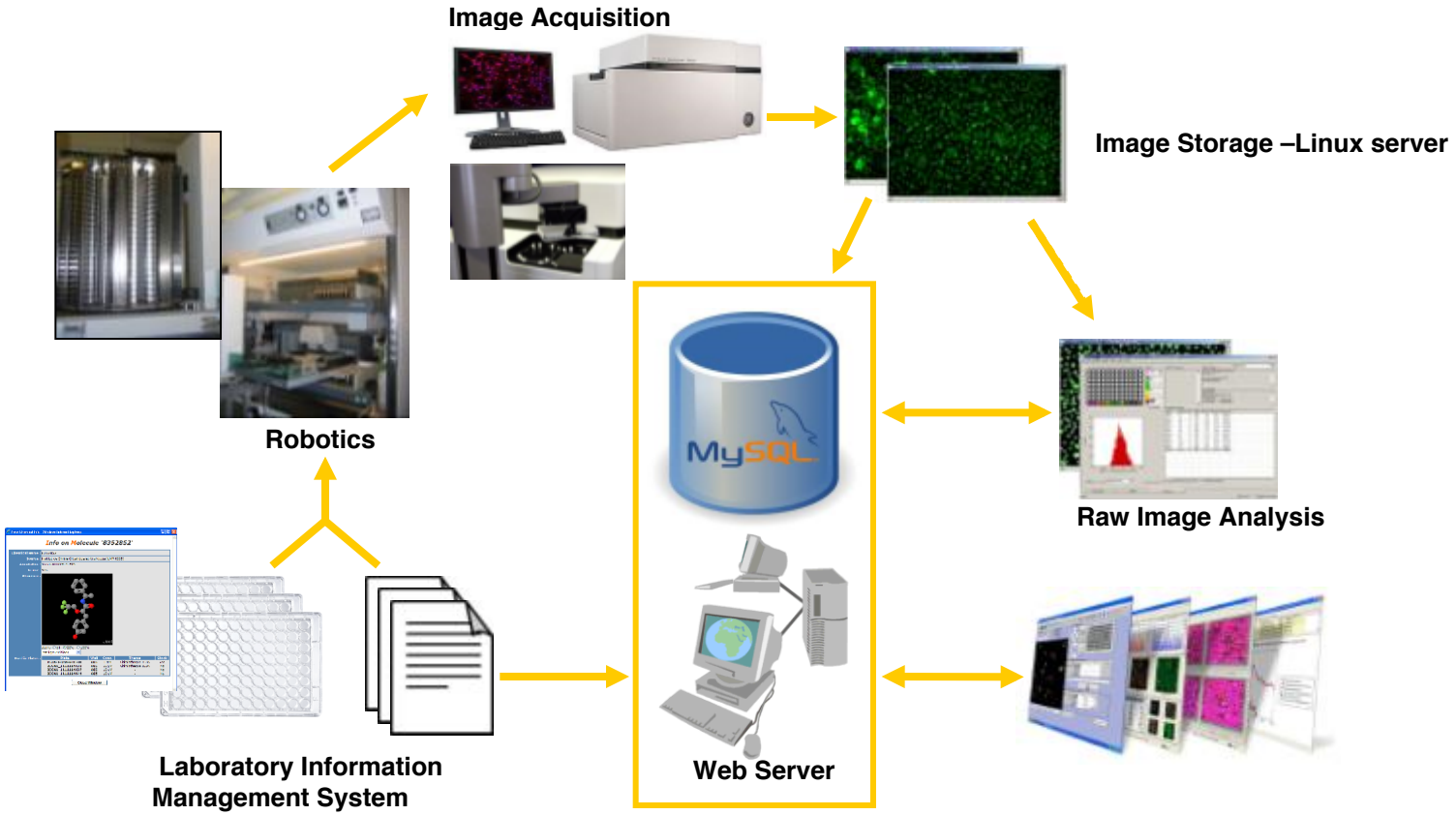
- **as a *validation* approach**
  (systematic depletion by siRNA, no *a priori*, just deplete)
- **as a *discovery* tool**
  (phenotypic clustering to identify pathways, systematic annotation)

Applied aim:

- **for *target validation***
  (toward tailored treatment)
- **for *drug discovery***
  (selection of effective drugs, prediction of "downstream" toxicity, improve effectiveness/toxicity ratio)

Strengths (the facility is 7 years-old)

The platform is equipped to handle all aspects of typical HCS screening workflow (siRNA and Chemical Libraries).



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Ensemble, prenons le cancer de vitesse

The Platform Team
(coll. with Bioinfo team)

Elaine DEL NERY
Platform Manager

Aurianne LESCURE
Automation Specialist

Sarah TESSIER
Elodie ANTHONY
Cellular Assays Development

Nabil AMIROUCHEN, MD
PhD Student
Oncologist

Grégory DUVAL
Web Developer

The scientific staff
(use the platform to their research)

Jacques CAMONIS
Research Director U830
Analysis of transduction pathways

Franck PEREZ
Research Director UMR 144
Microtubule Dynamics and Intracellular Trafficking

Philippe BENAROCH
Research Director U932
Intracellular Transport & Immunity

- Introduction and strengths of our facility/research group

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How the researcher arrives to us ?

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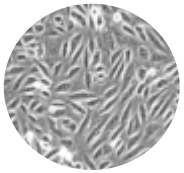
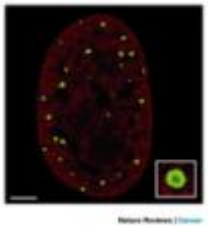
Scientific question

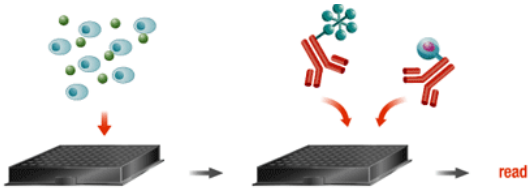


Cell model



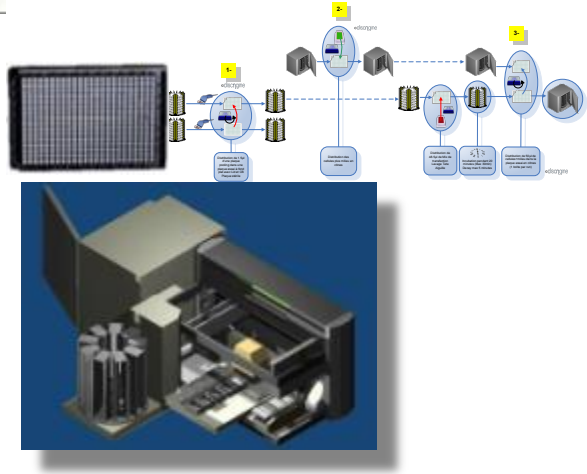
Tools to detect the target of interest/or cell structure

Miniturization steps in 96-well plates



- Optimal cell density
- siRNA transfection efficiency
- DMSO sensibility
- Others: biotin, IL-1, arsenic addition
- Immunofluorescence protocol
- Check assay controls

Miniturization steps in 384-well plates



From bench to robotics

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How long does it take to run a screening project ?

3-6 months

1-3 months

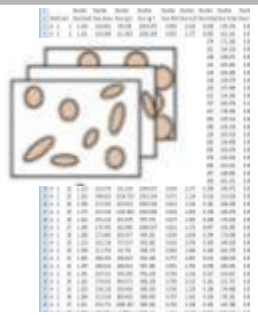
Few weeks - 3 months

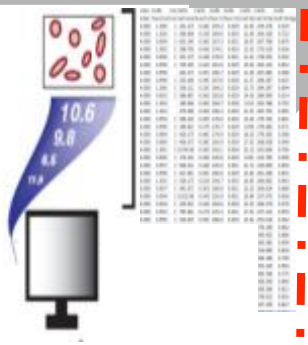
Screen campaings

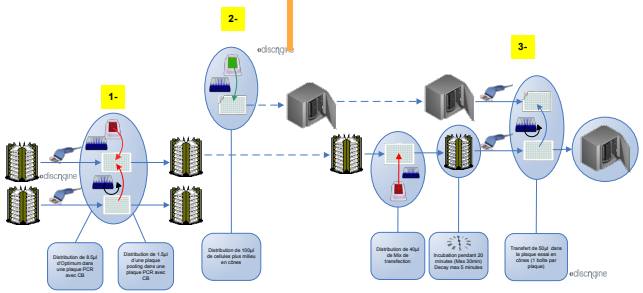
checks

Projects running at dif. levels

- Project feasibility.
- Miniaturization







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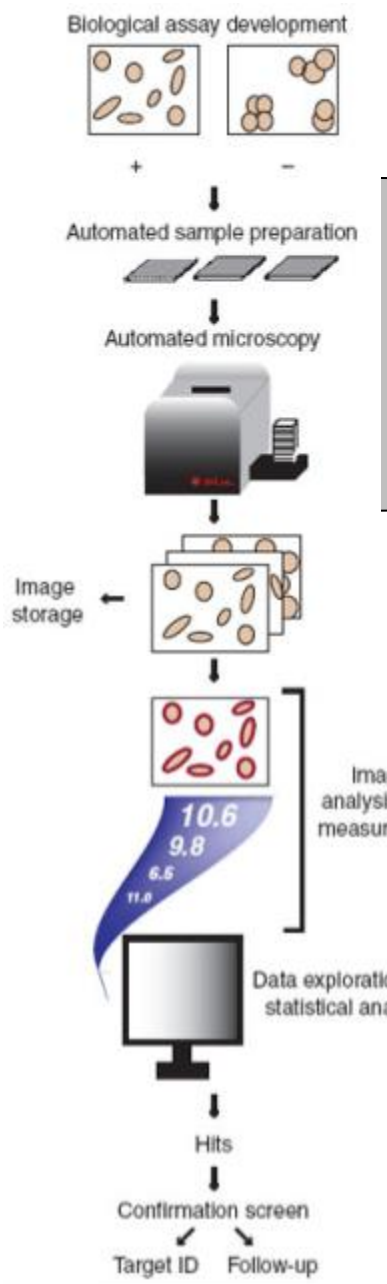
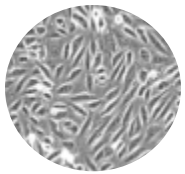
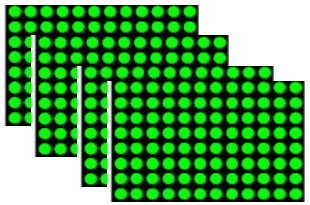
High-Content Screening Platform

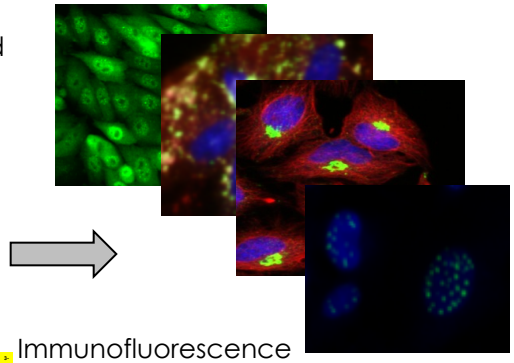


siRNA Library or chemicals (4 siRNAs/gene)

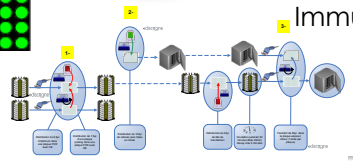




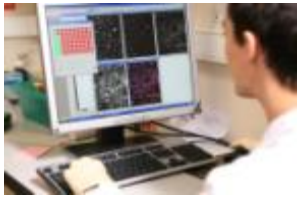
Other compounds added (TNF-α, arsenic, IL-1 …)

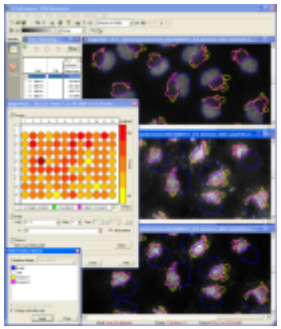


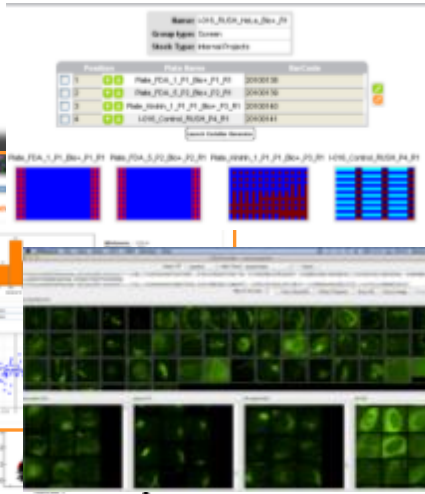
Immunofluorescence

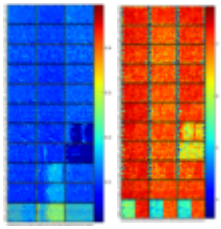


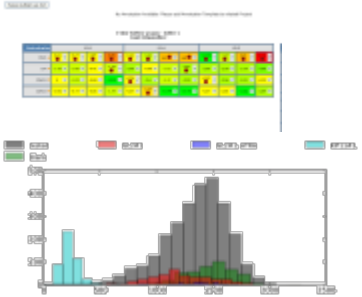
Data exploration and analysis

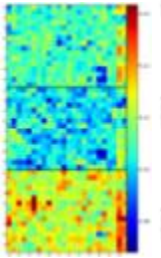


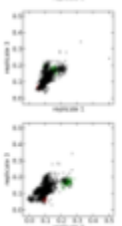












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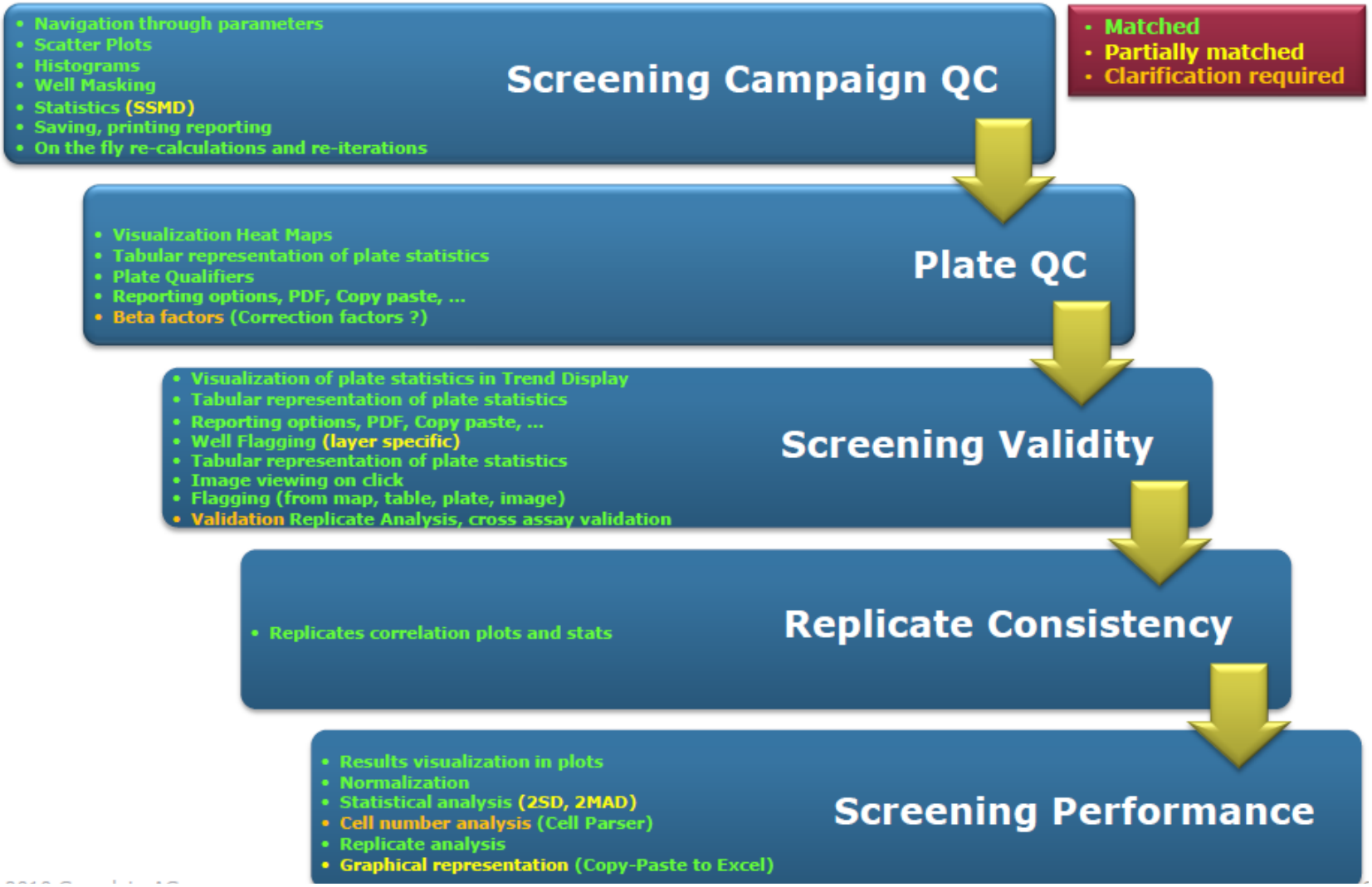
Work in progress – by levels

Level 1 : Data organization and processing steps (a central challenge)



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Work in progress

Level 2 : High-level exploration of phenotypic data

Population analysis

Validate results, weed out noise and redundant data, increase internal consistency

- Descriptive statistics
- Correlation analysis
- 1v1 distributions

Outlier detection

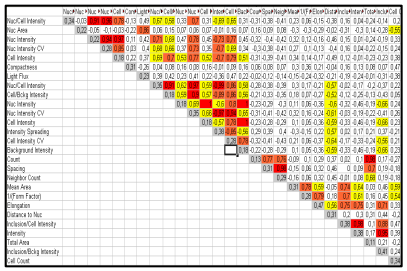
Highlight possible targets in global space or subspace of interest, perform preliminary clustering

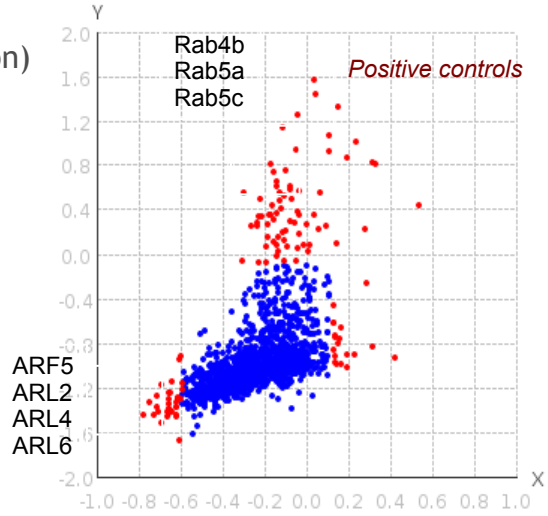
- PCA, ICA

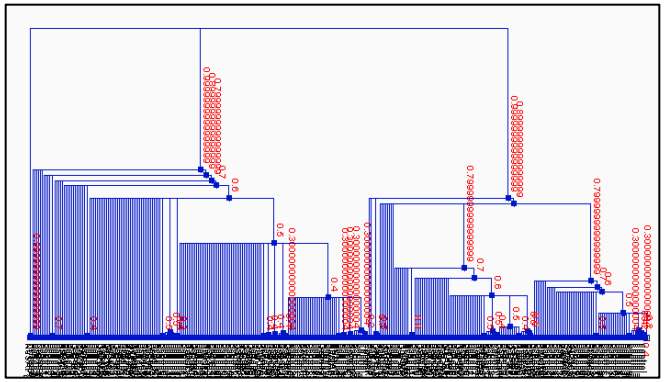
Multiparametric Clustering

Detect fingerprinting profiles, local and global similarities in a unified environment

- Hierachical Clustering
- DBSCAN (density-based)
- CLIQUE (subspace exploration)







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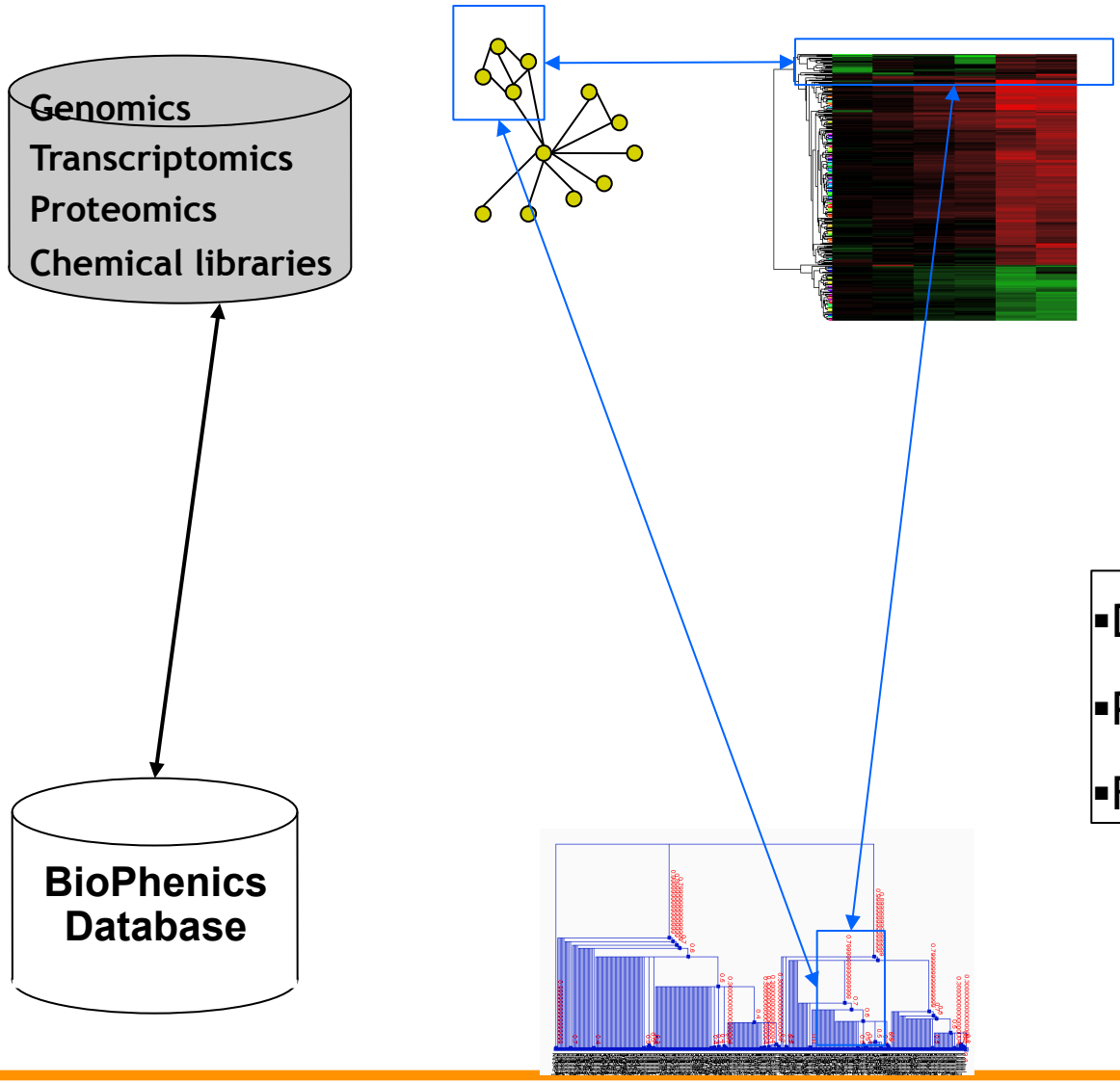
Future work

Level 3: Towards data integration



- Data cross-validation
- Pattern discovery
- Functional annotation

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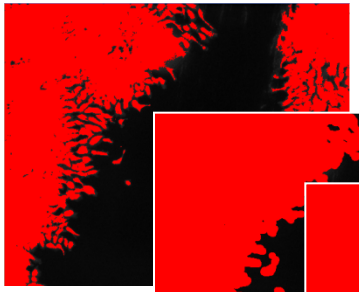
Develop Image segmentation is a permanent need

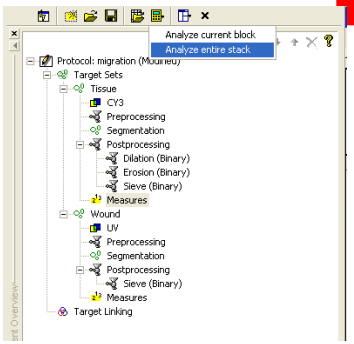
Intensity segmentation



Binary dilation

erosion

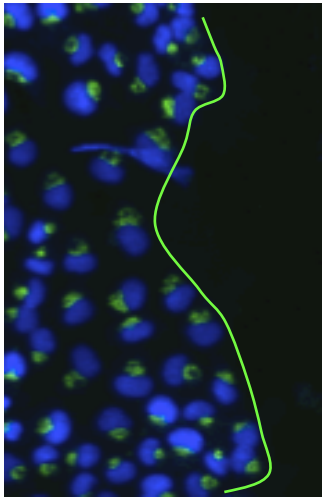
sieving of ‘orphaned’ spots.

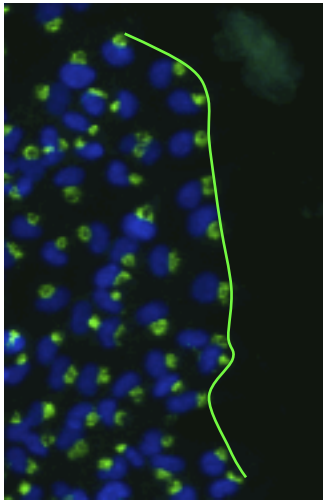


Define ‘wound’ area

Multi-color edge detection

Migration and polarization quantification





Cell Migration

Cell Polarization

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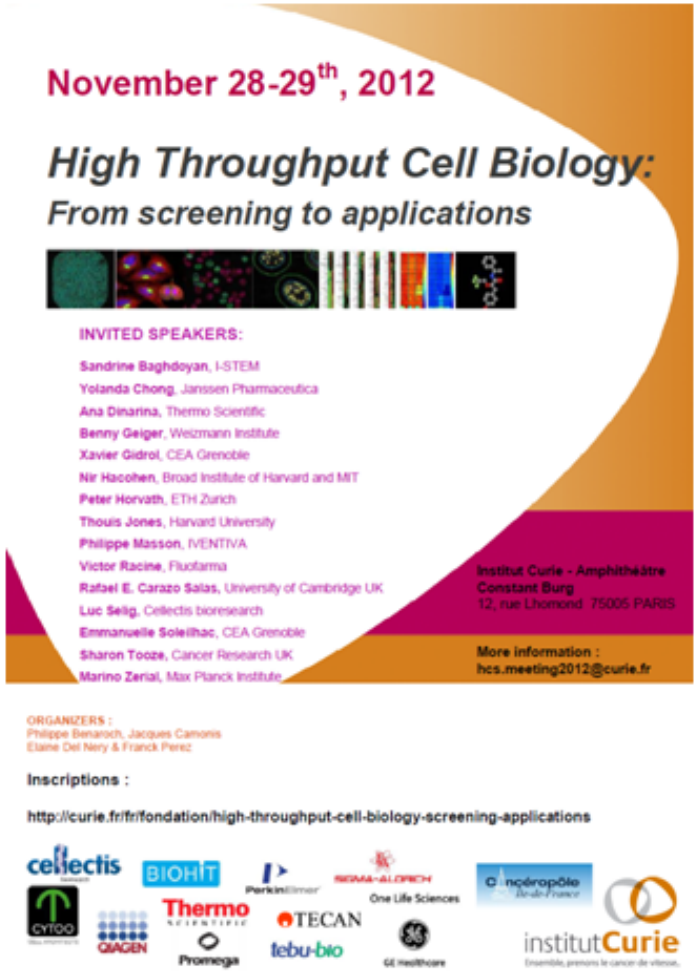
Education

- **Meeting organization**

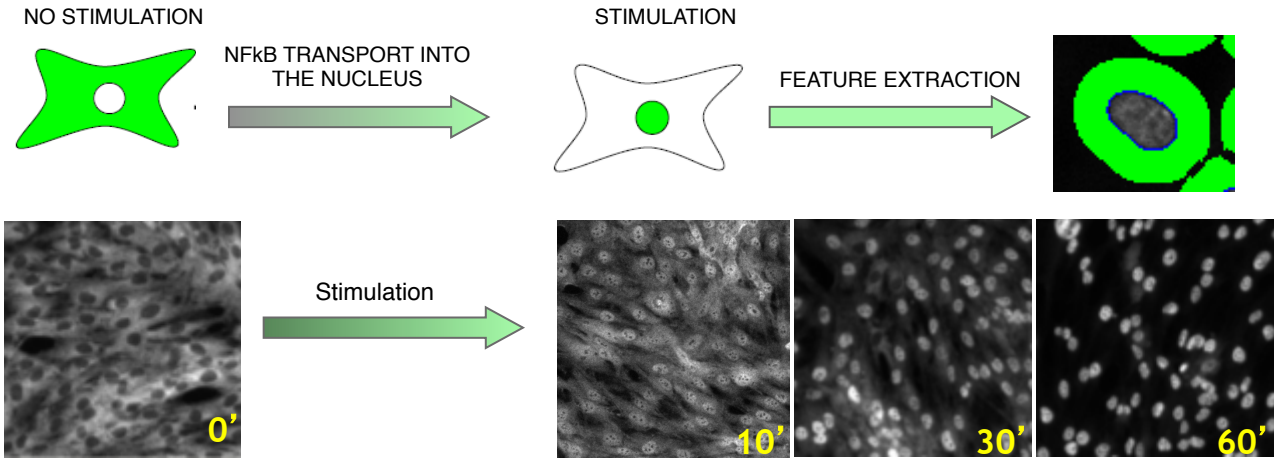
Two-day meeting - 170 people for all over Europe, no fee



Collaboration: basically french research groups and small pharma

Philippe Benaroch's group

Role of cysteine proteases in TLR3 signalling



PNAS

Cleavage of Toll-like receptor 3 by cathepsins B and H is essential for signaling

Alejandra Garcia-Cattaneo[a,b], François-Xavier Gobert[a,b], Mélanie Müller[a,c], Florent Toscano[d], Marcella Flores[a,b], Aurianne Lescure[a,c], Elaine Del Nery[a,c], and Philippe Benaroch[a,b,1]

[a]Institut Curie, Centre de Recherche, 75005 Paris, France; [b]Institut National de la Santé et de la Recherche Médicale, Unité 932, 75005 Paris, France; [c]Institut Curie, Translational Department, BioPhenics Platform, Hôpital Saint Louis, 75010 Paris, France; and [d]Centre de Recherche en Cancérologie de Lyon, Institut National de la Santé et de la Recherche Médicale, Unité Mixte de Recherche 5286/Centre National de la Recherche Scientifique, 69008 Lyon, France

Edited by Ira Mellman, Genentech, Inc., South San Francisco, CA, and approved April 18, 2012 (received for review September 15, 2011)

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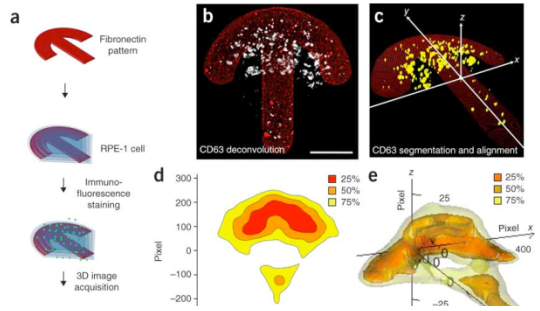
Some Projects from Lab Bench to BioPhenics

Towards the understanding of cell organisation

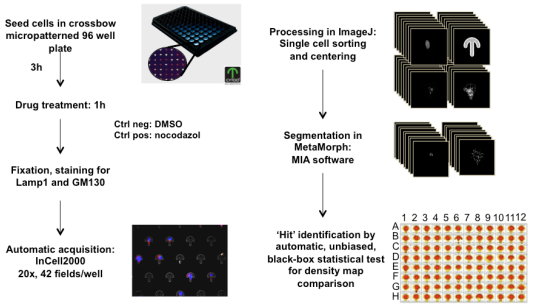
560 | VOL.7 NO.7 | JULY 2010 | NATURE METHODS

Probabilistic density maps to study global endomembrane organization

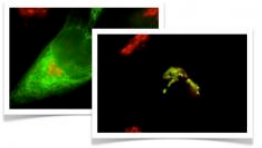
Kristine Schauer & Bruno Goud



Density-based approach in micropatterned cells towards quantitative analysis of cellular organization in high-content approaches.



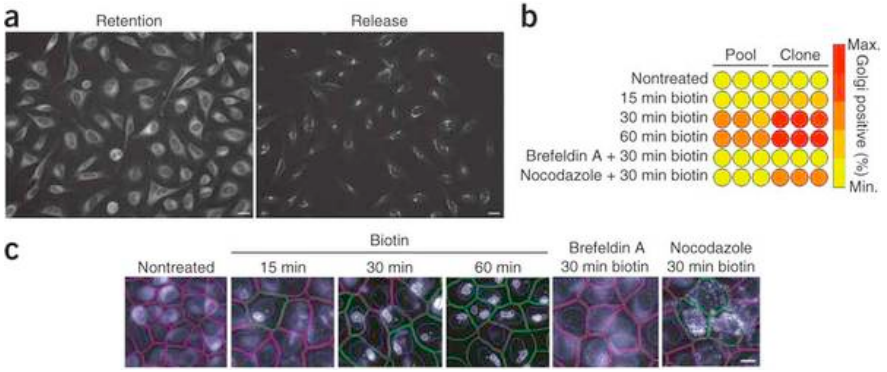
Regulated secretion
RUSH (Retention Using selective Hook)



ADVANCE ONLINE PUBLICATION | NATURE METHODS

Synchronization of secretory protein traffic in populations of cells

Franck Perez's group



The RUSH SYSTEM to understand the mechanisms of trafficking and enable screens for molecules that perturb pathological protein transport

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