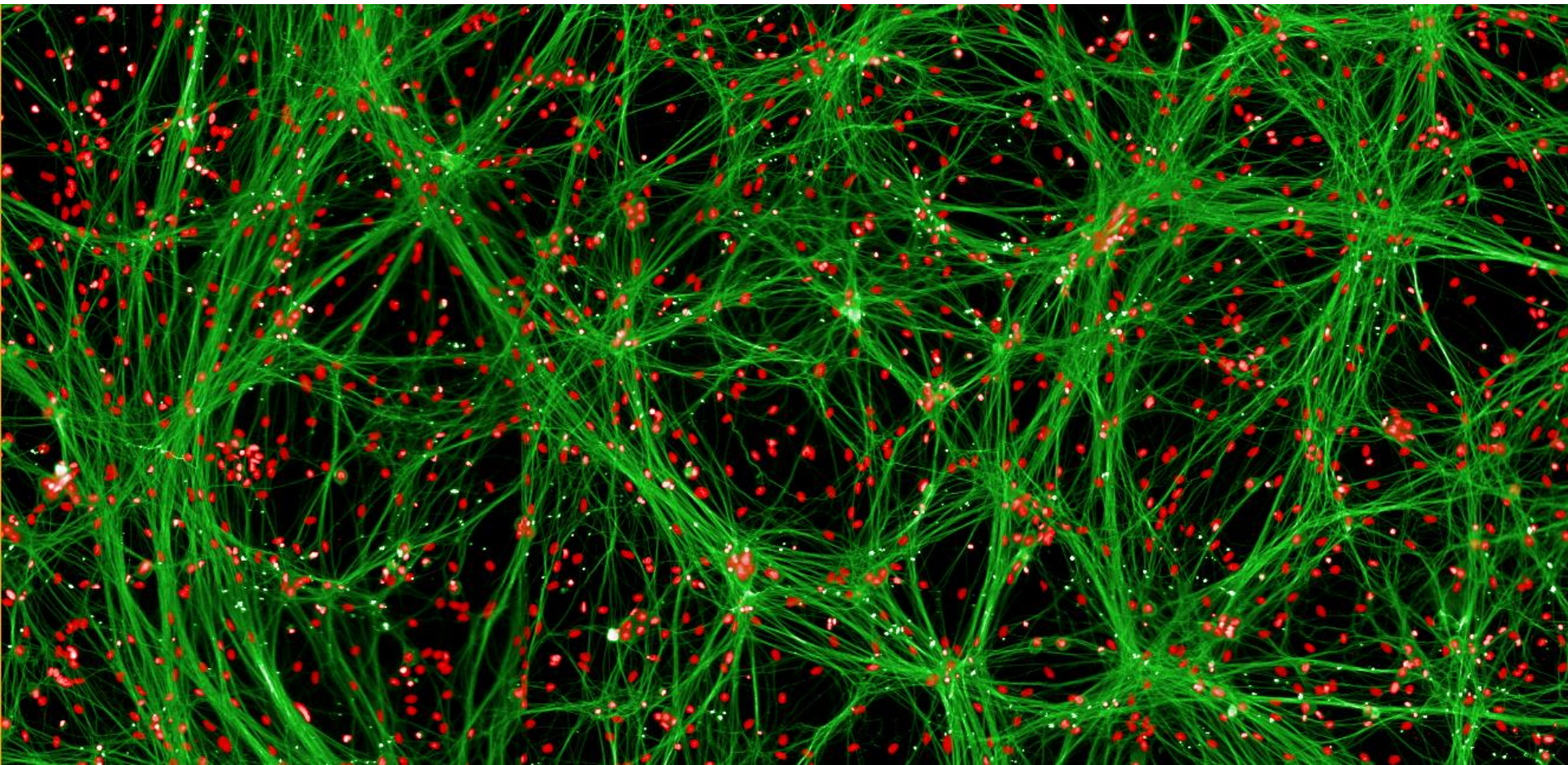
高内涵细胞影像信息学技术

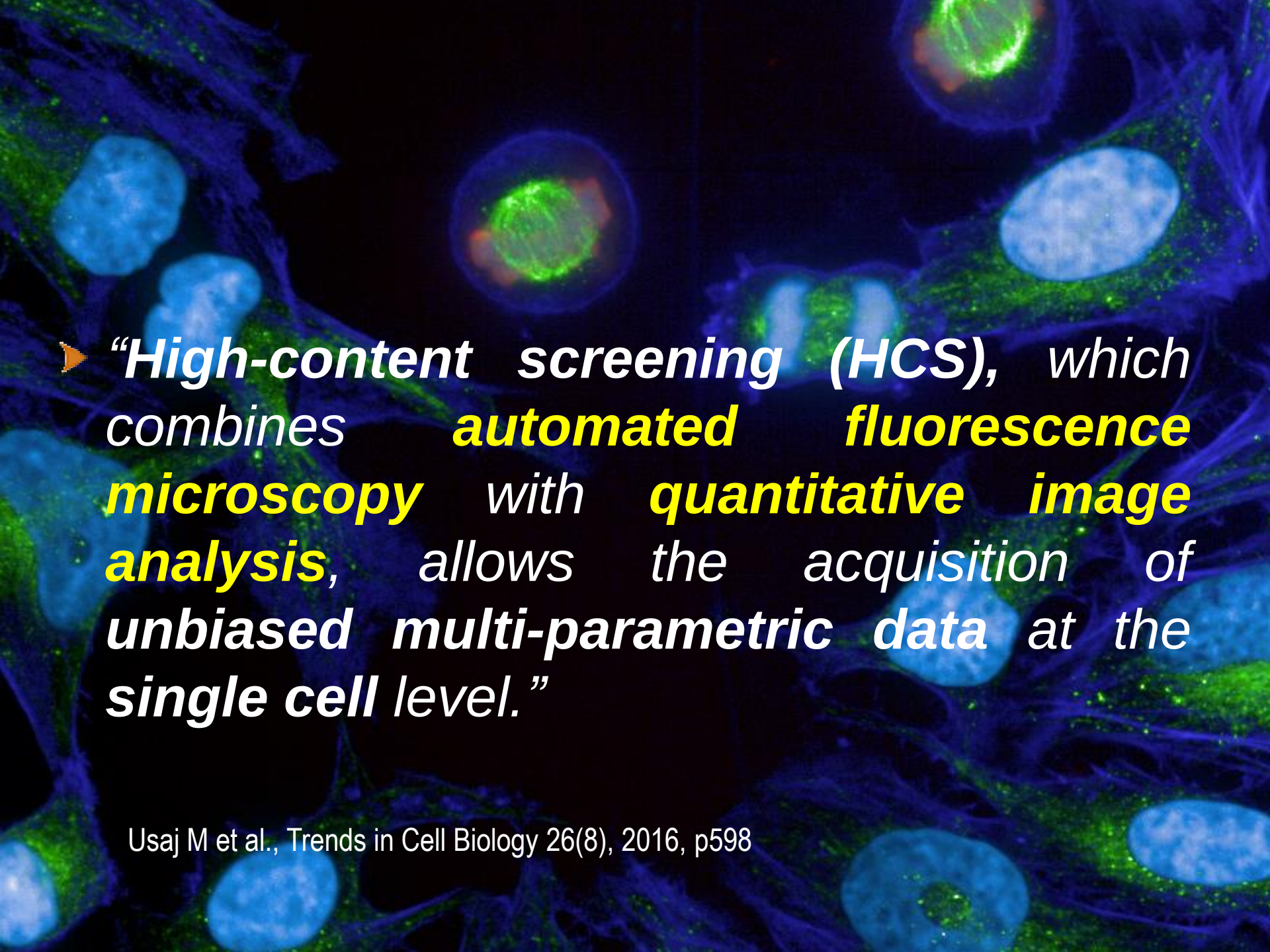
——由图像采集迈向数据挖掘

技术支持　　于雪梅

济南友泽仁信贸易有限公司



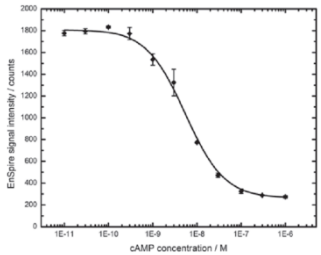
PerkinElmer覆盖分子、细胞、动植、组织一系列产品

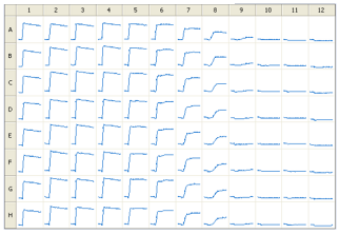


- *"**High-content screening (HCS),** which combines **automated fluorescence microscopy** with **quantitative image analysis**, allows the acquisition of **unbiased multi-parametric data** at the **single cell** level."*

Usaj M et al., Trends in Cell Biology 26(8), 2016, p598

什么是高内涵？



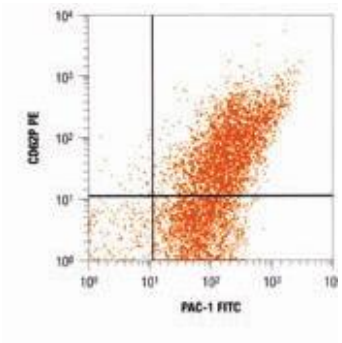


酶标仪

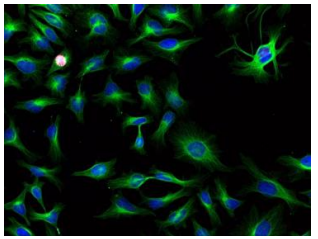
高通量

成像

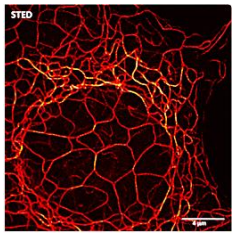
流式细胞仪



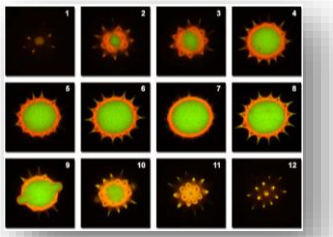
荧光显微镜



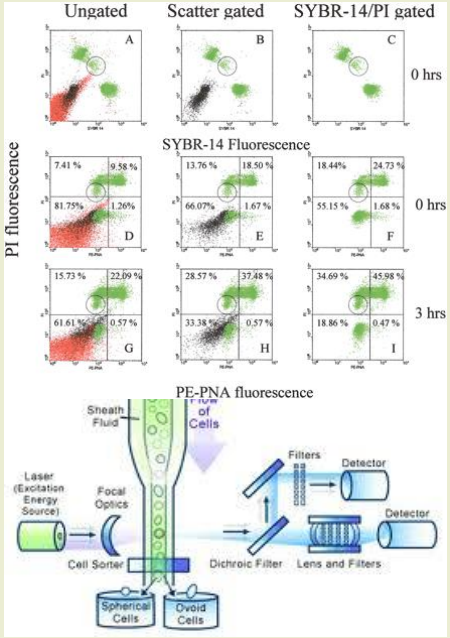
超高分辨



共聚焦



共聚焦技术vs. 流式细胞技术vs. 高内涵技术



流式细胞技术（消化细胞）

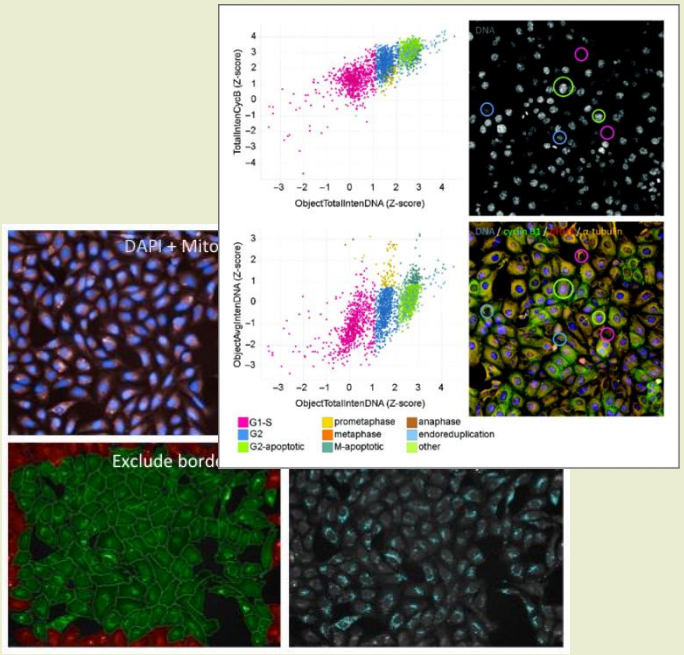
- 血液或其他液体
- 消化后的组织样品
- 样品消耗量大
- 精确的细胞水平定量结果

无亚细胞结构信息

激光共聚焦（玻片）

- 样本准备量大、试剂消耗量大
- 清晰的亚细胞结构图像
- 成像耗时长、效率低
- 简单细胞定量

无客观批量的定量结果



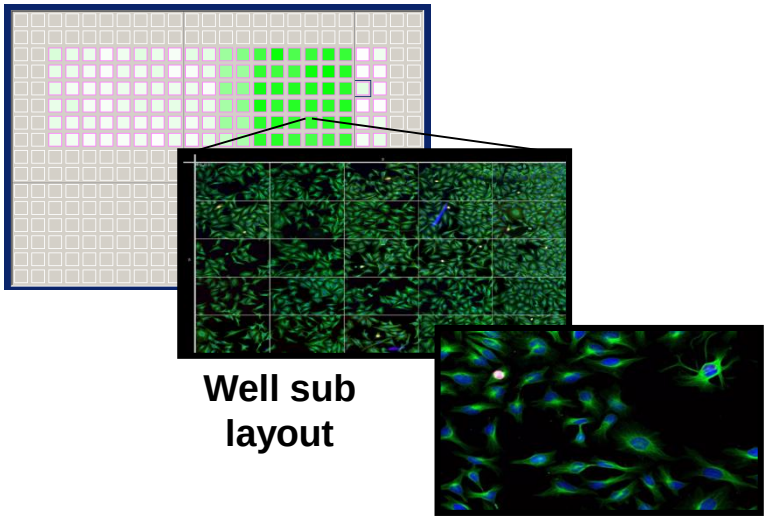
高内涵技术（孔板）

- 成像实验设计体系完整
- 清晰的亚细胞结构图像
- 精细单细胞、细胞器水平分析
- 丰富的细胞器水平软件自动算法
- 客观高效的批量数据统计结果

基于亚细胞结构的客观批量单细胞定量

高内涵的工作流程:

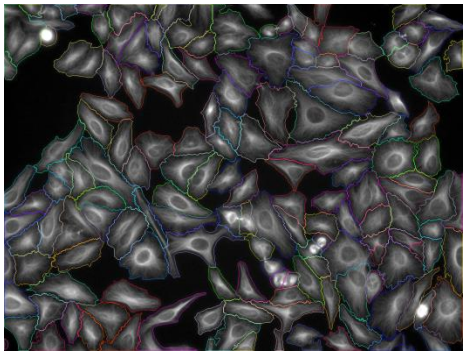
1. 自动扫描

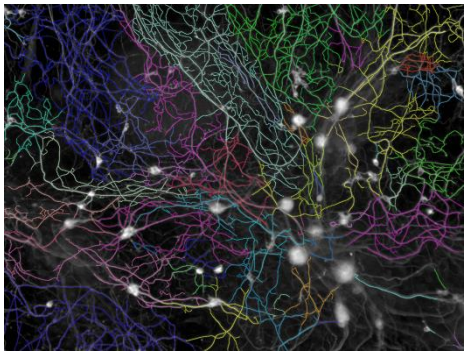


Well sub layout

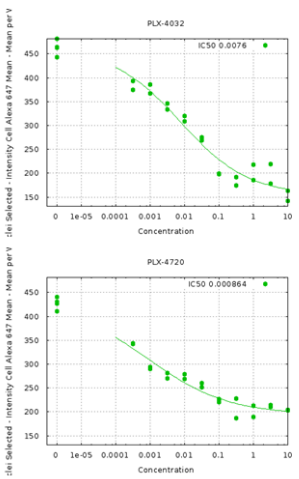
Multi color image field

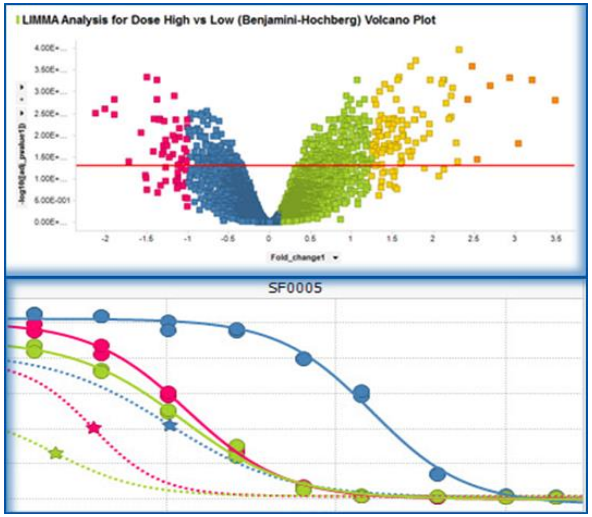
2. 图像分析





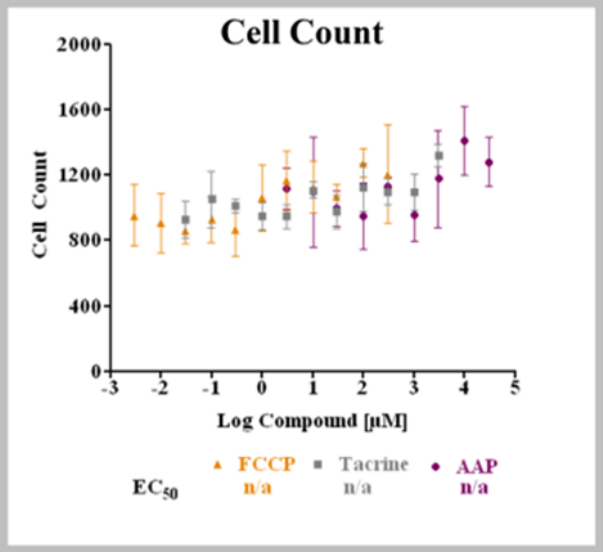
3. 数据可视化及数据挖掘





单细胞形态获取 + 流畅自动使用过程

A



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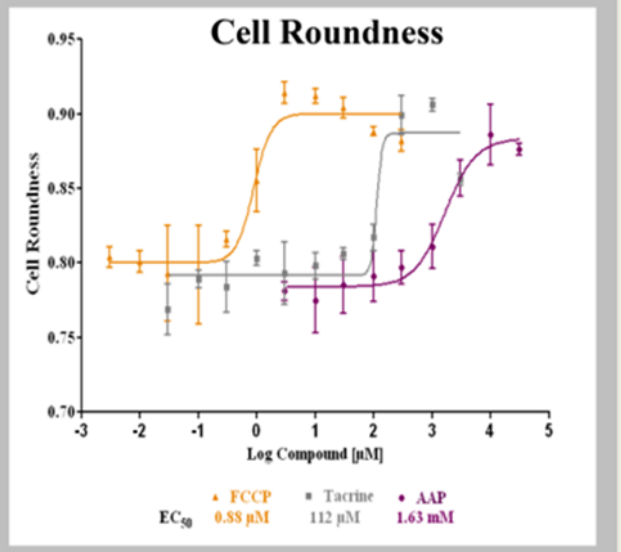

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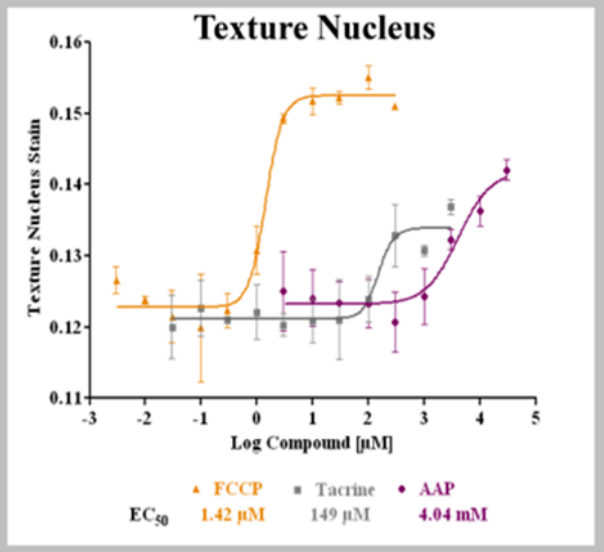

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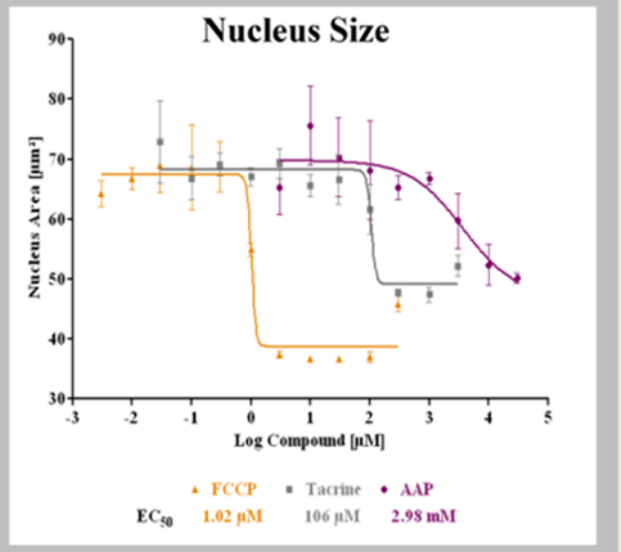

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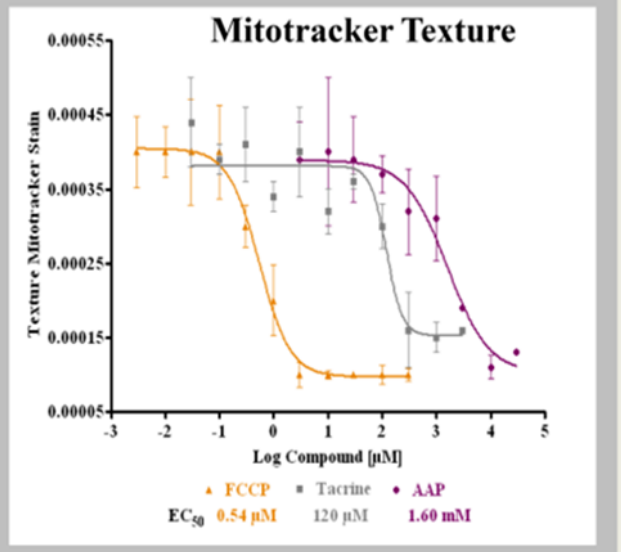
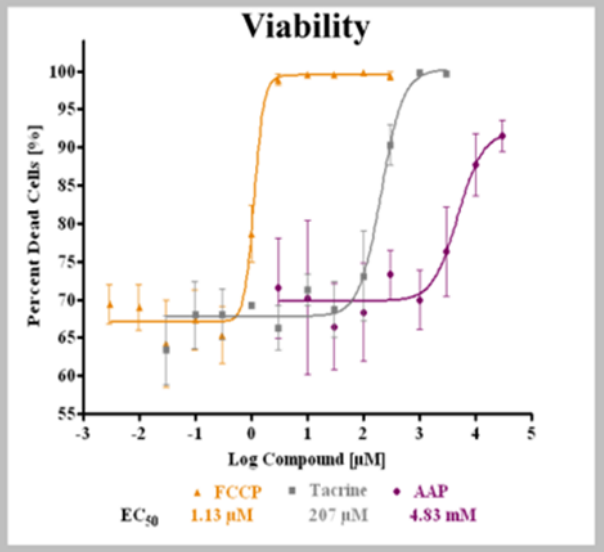
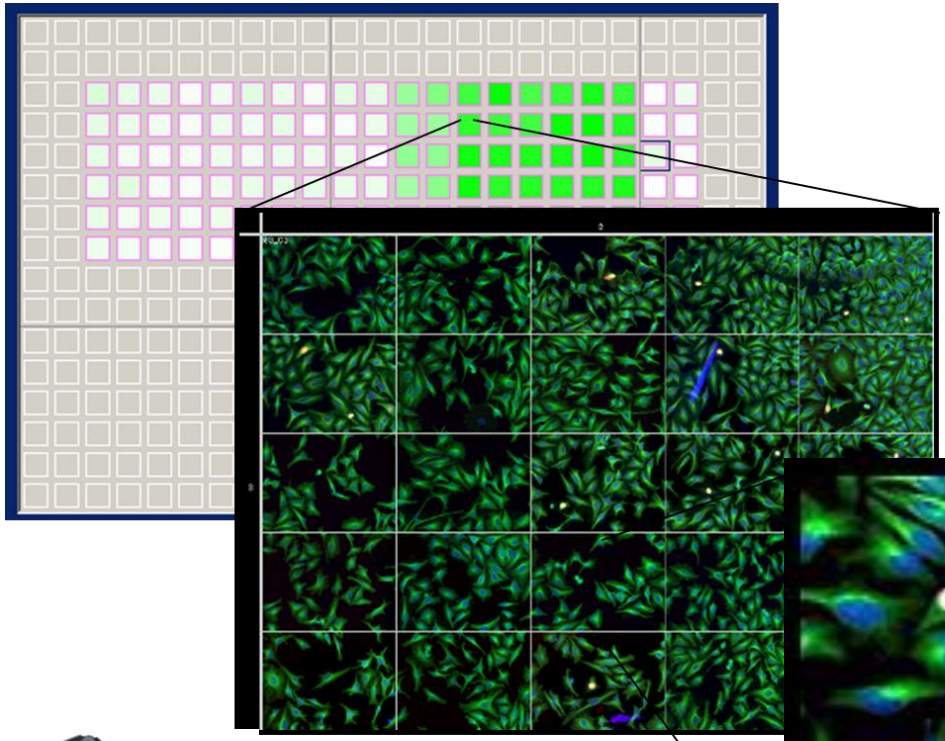


F

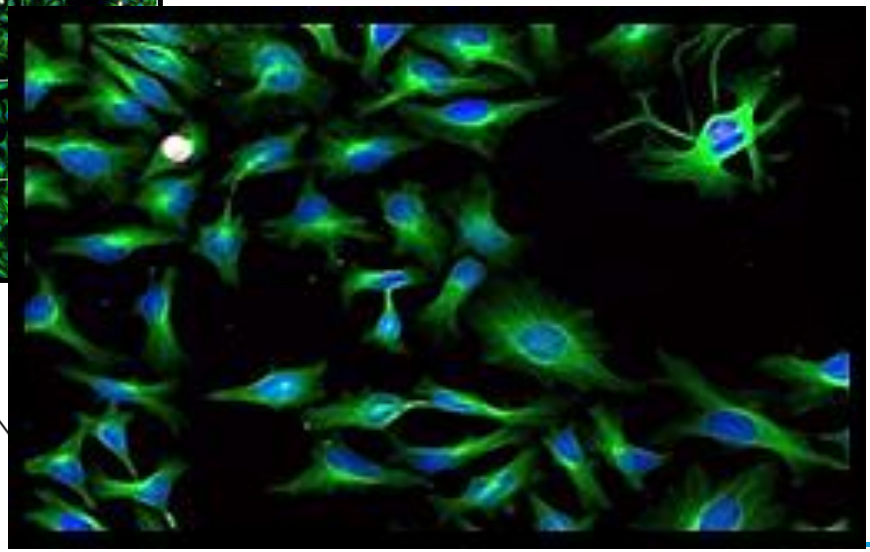


高内涵提供平行采样，提供更准确的细胞信息

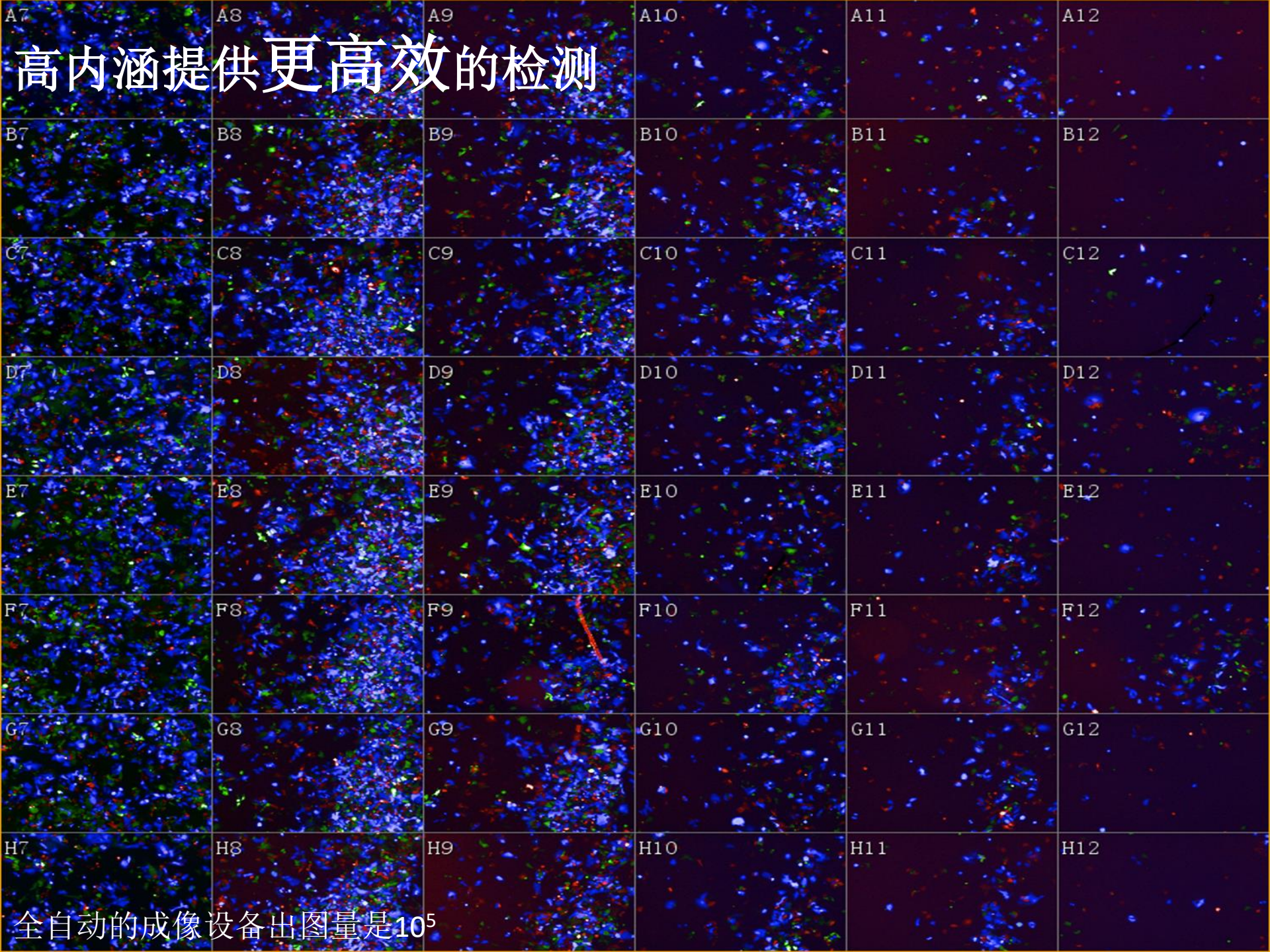
- High Content Screening is single cells based and Multi-parameter outputs

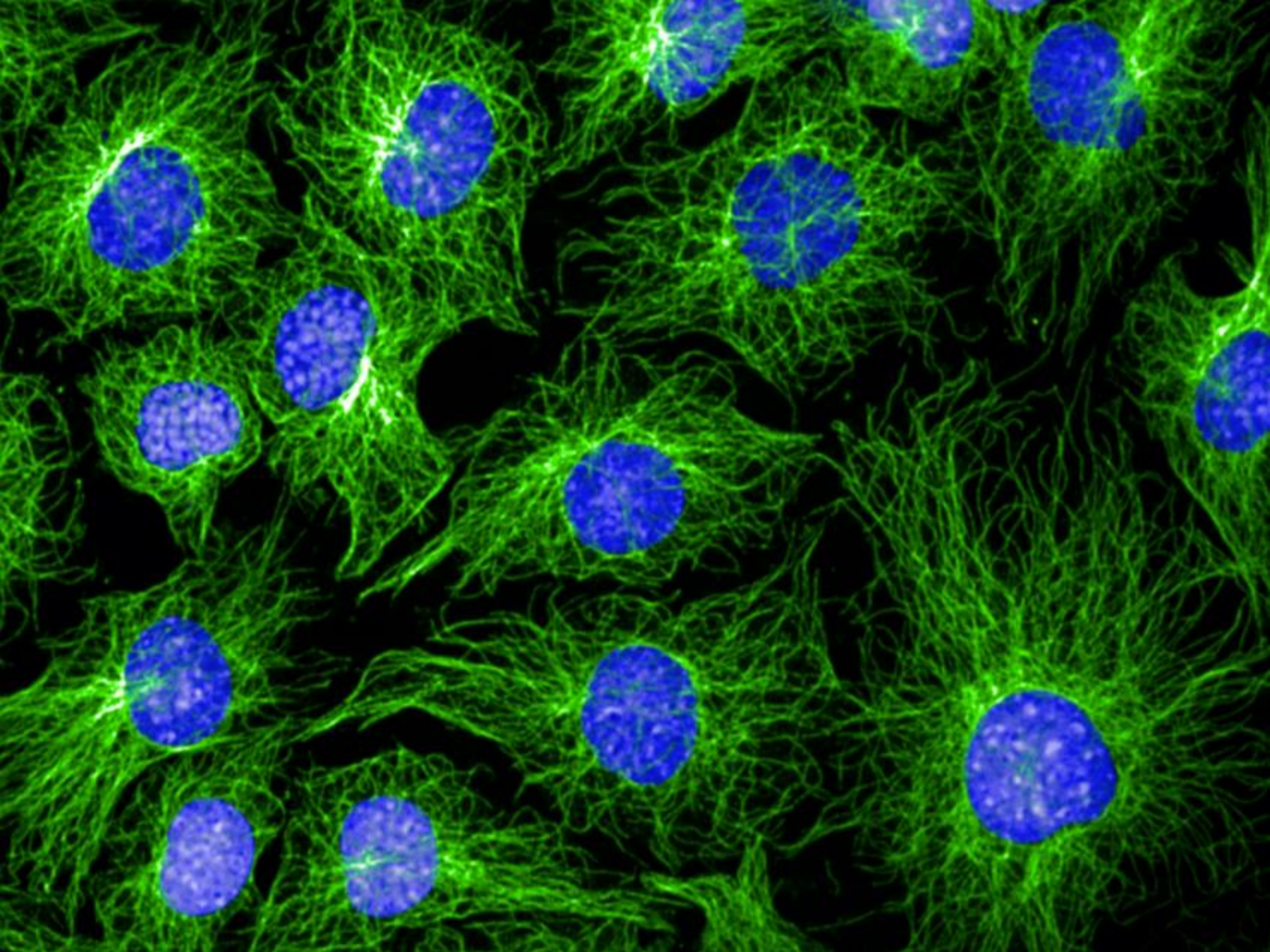


Multi color image field

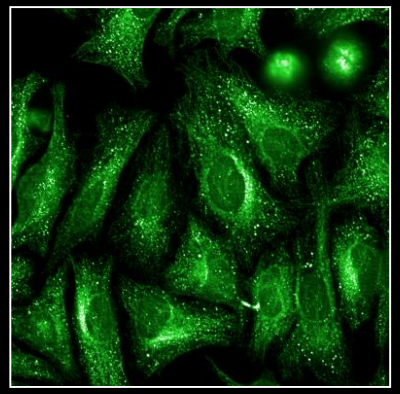


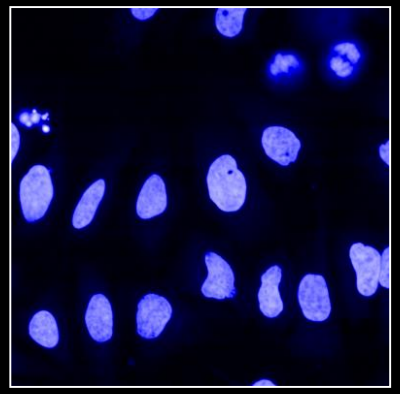
Vell sub layout

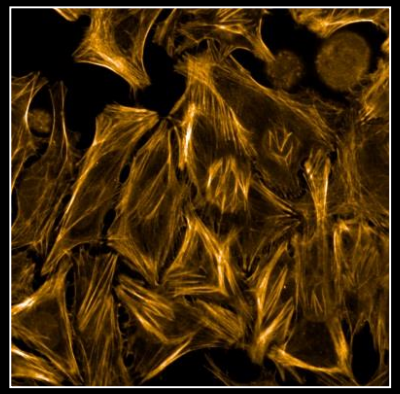

高内涵提供更高效的检测
A7
A8
A9
A10
A11
A12
B7
B8
B9
B10
B11
B12
C7
C8
C9
C10
C11
C12
D7
D8
D9
D10
D11
D12
E7
E8
E9
E10
E11
E12
F7
F8
F9
F10
F11
F12
G7
G8
G9
G10
G11
G12
H7
H8
H9
H10
H11
H12
全自动的成像设备出图量是10^5

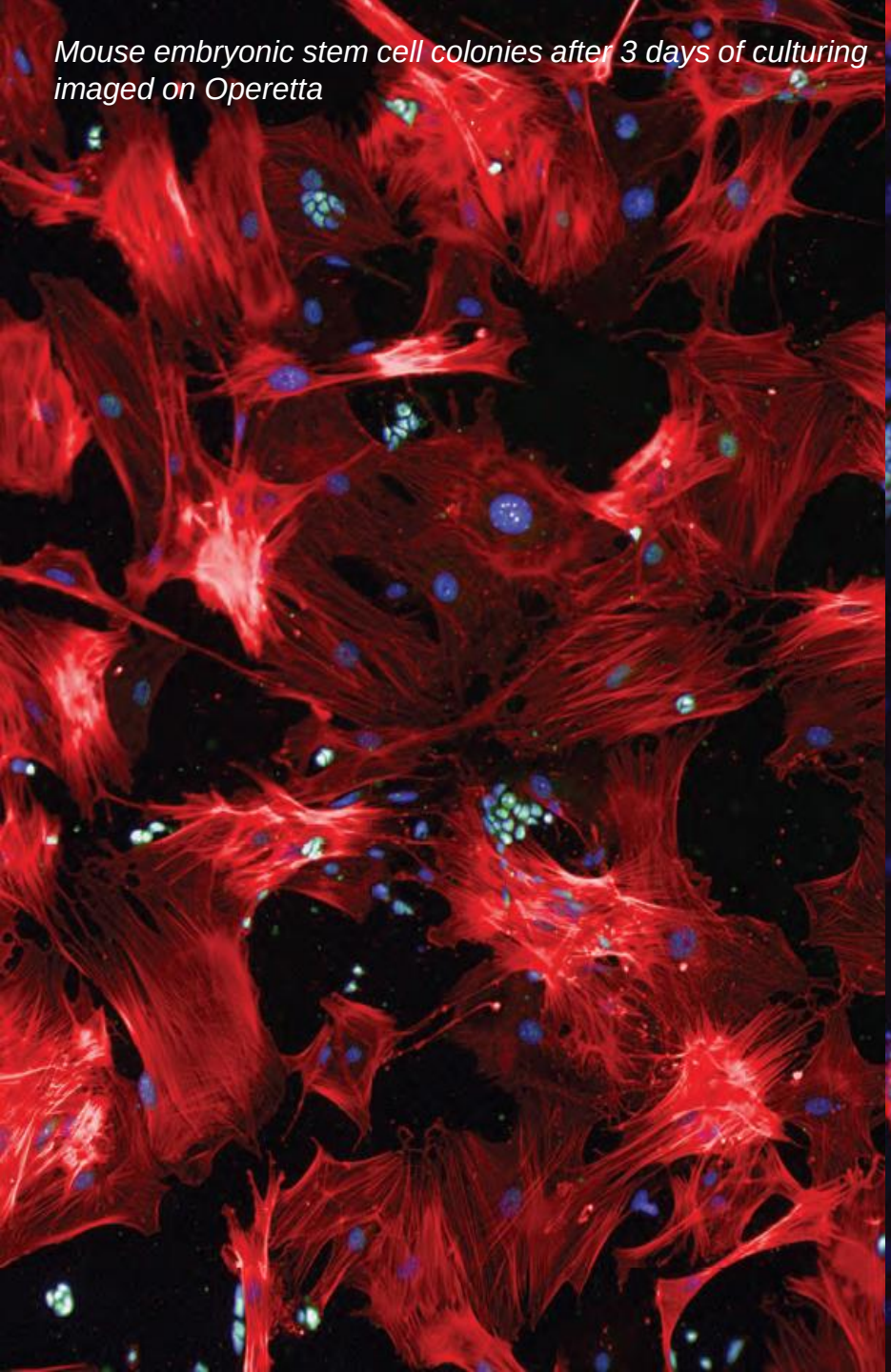


63x Water (NA 1.15)
Confocal

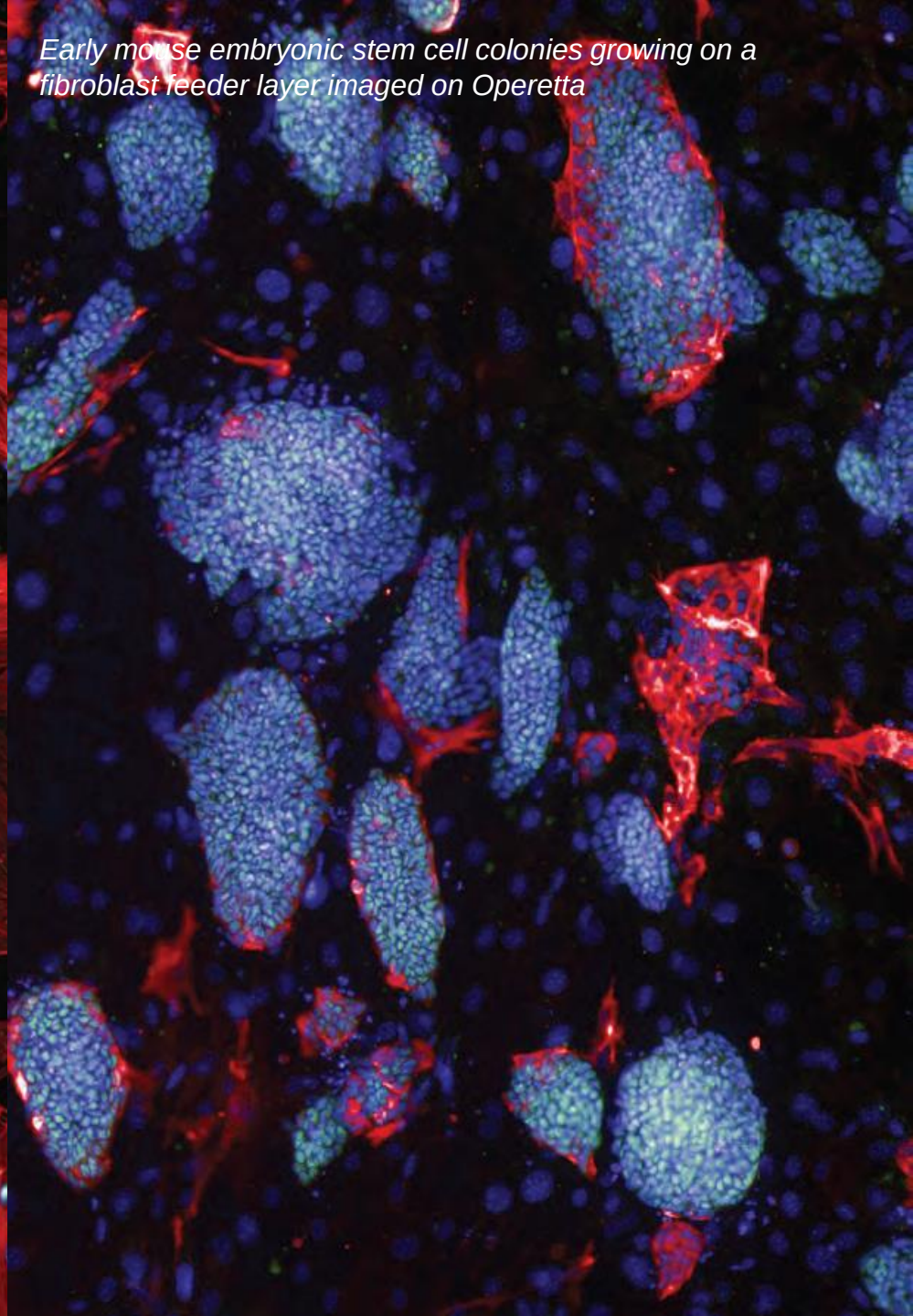




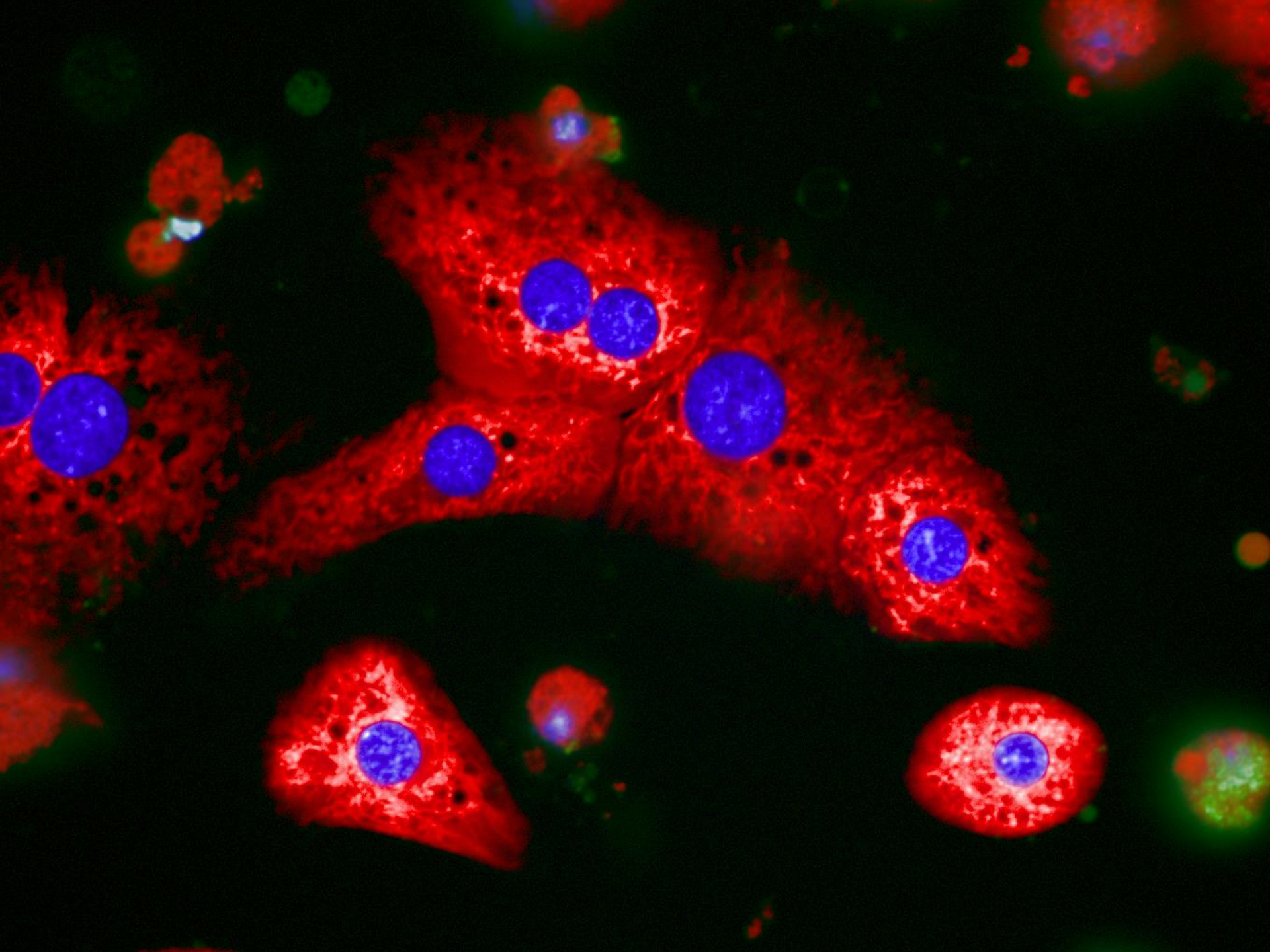


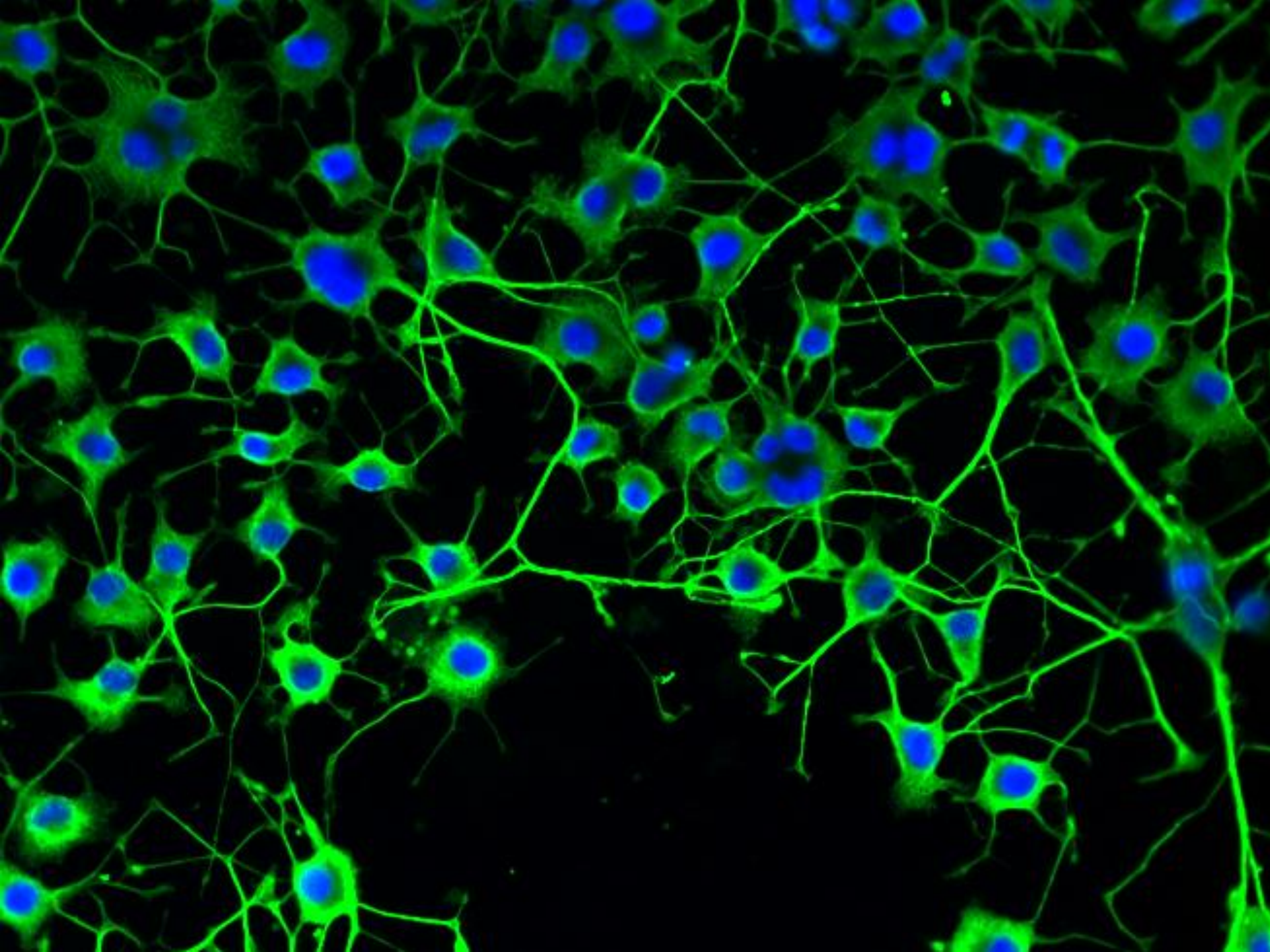


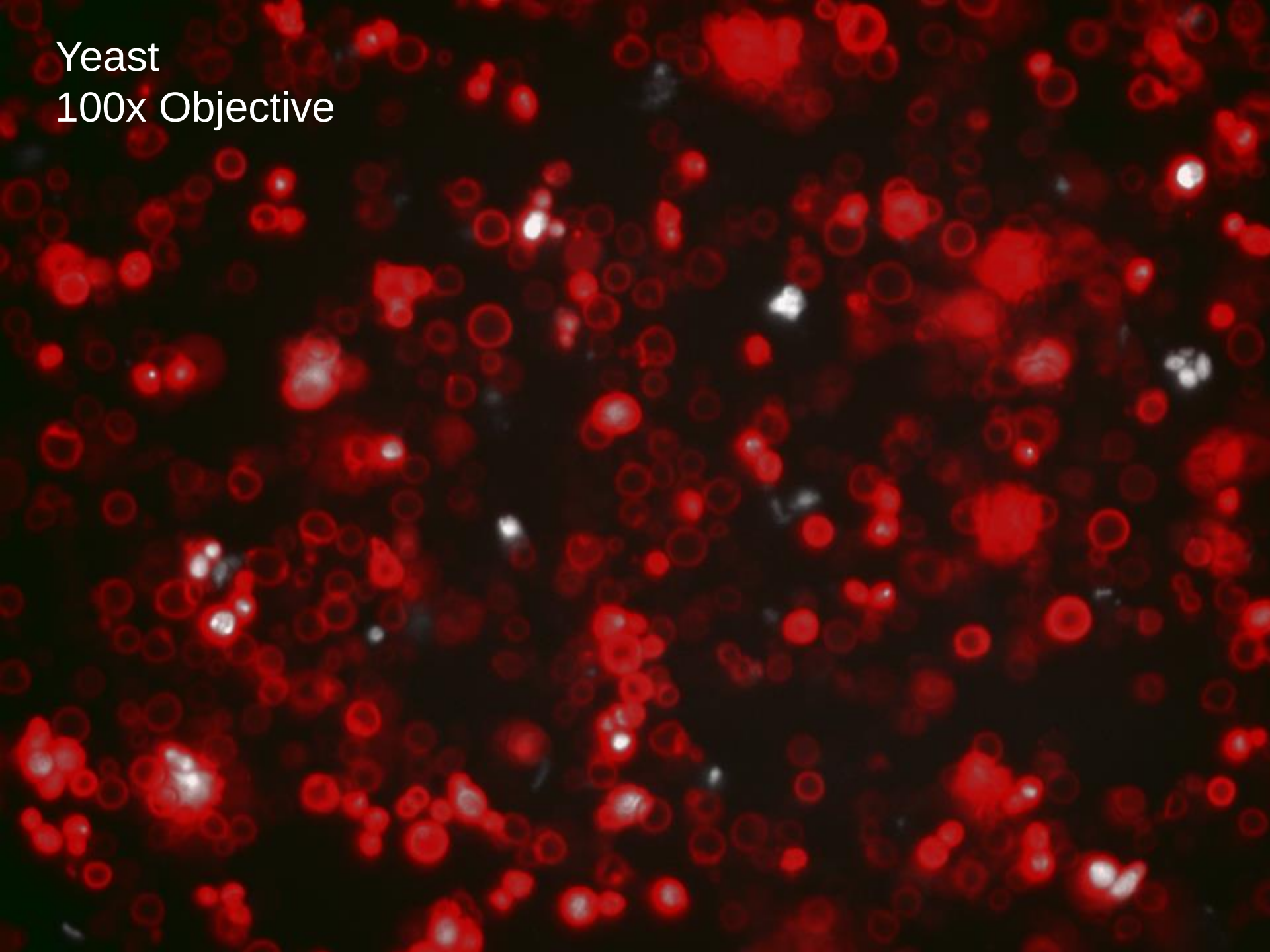
Mouse embryonic stem cell colonies after 3 days of culturing imaged on Operetta



Early mouse embryonic stem cell colonies growing on a fibroblast feeder layer imaged on Operetta





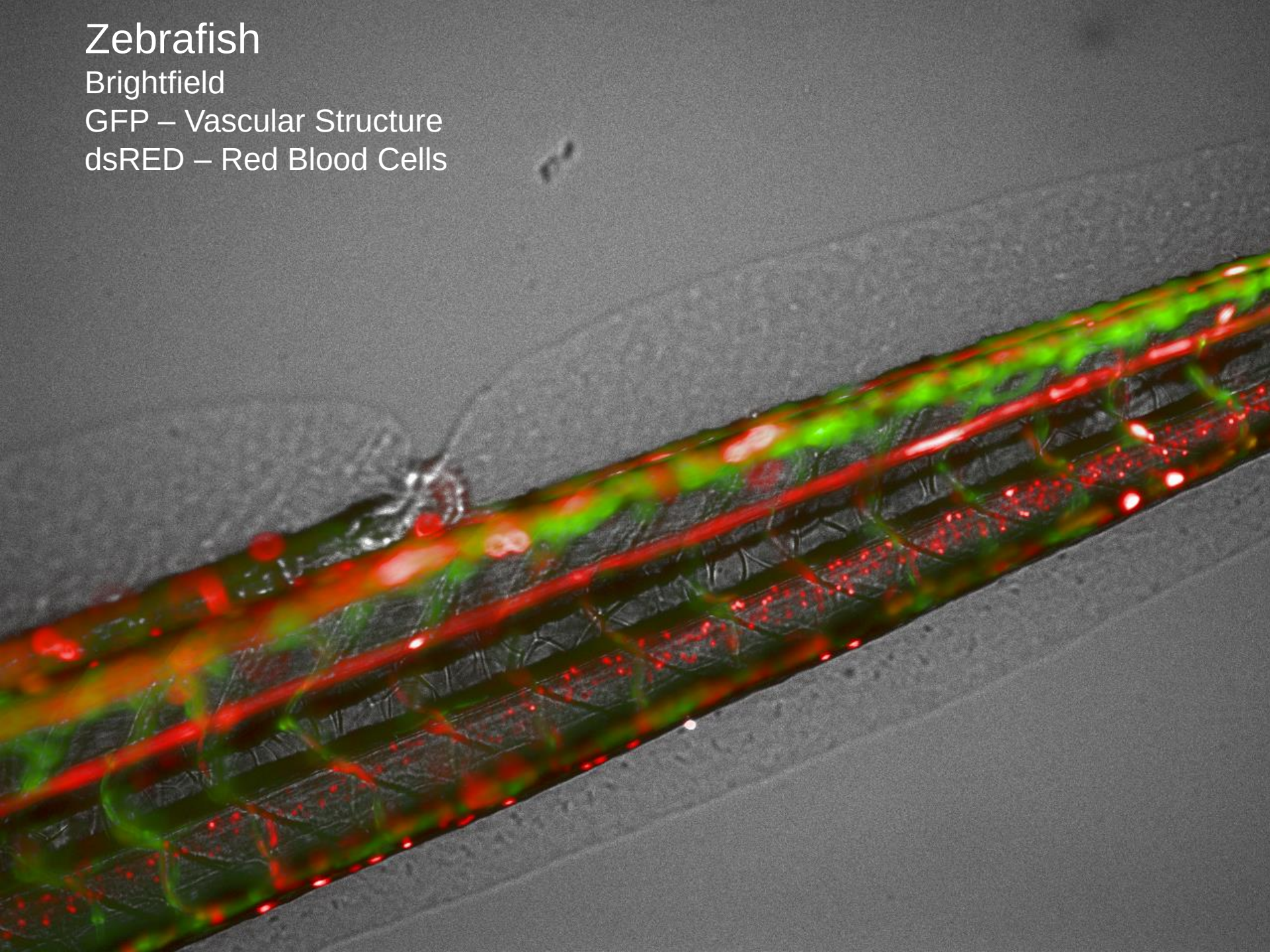

Yeast
100x Objective

Zebrafish

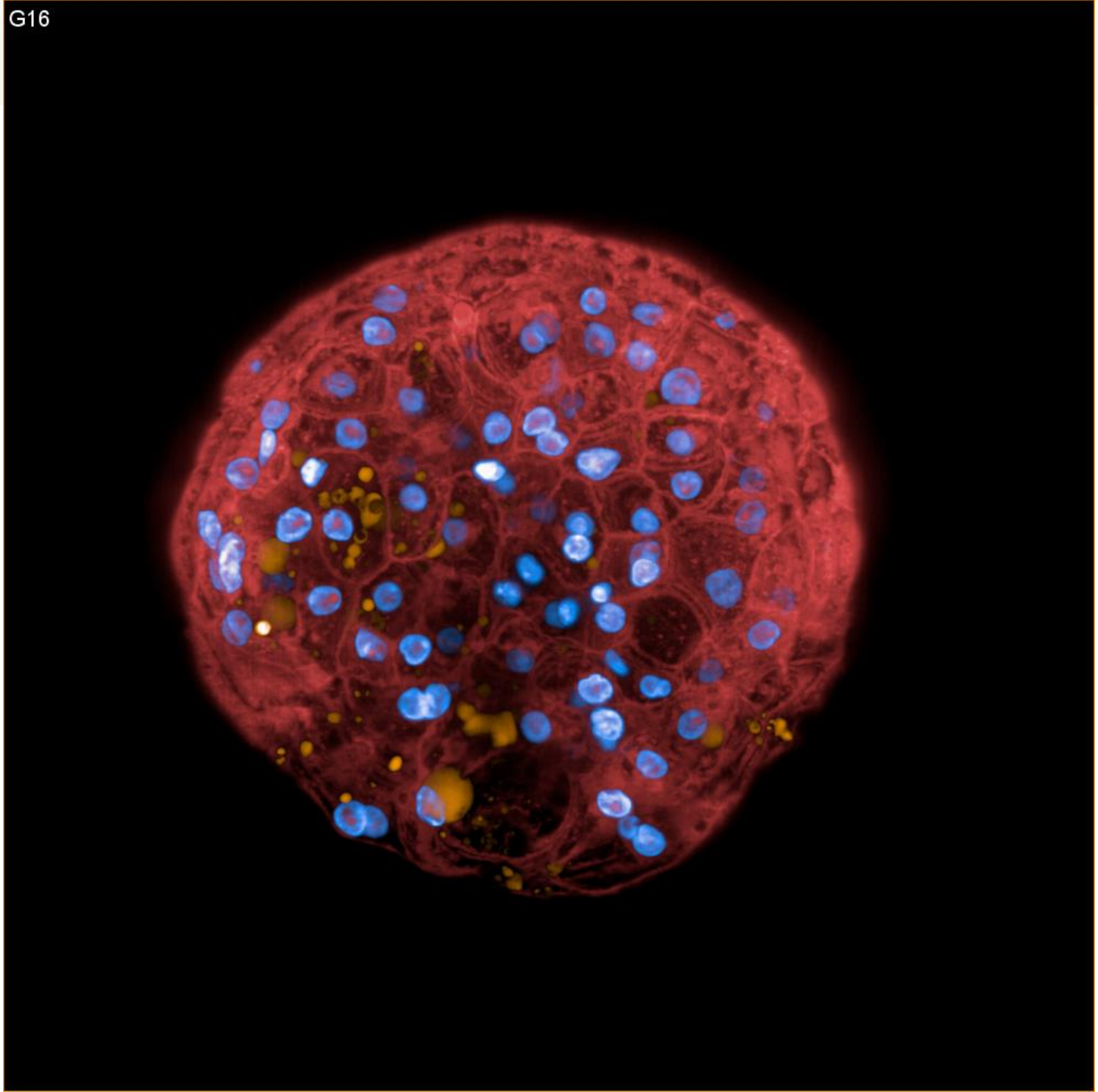
Brightfield

GFP – Vascular Structure

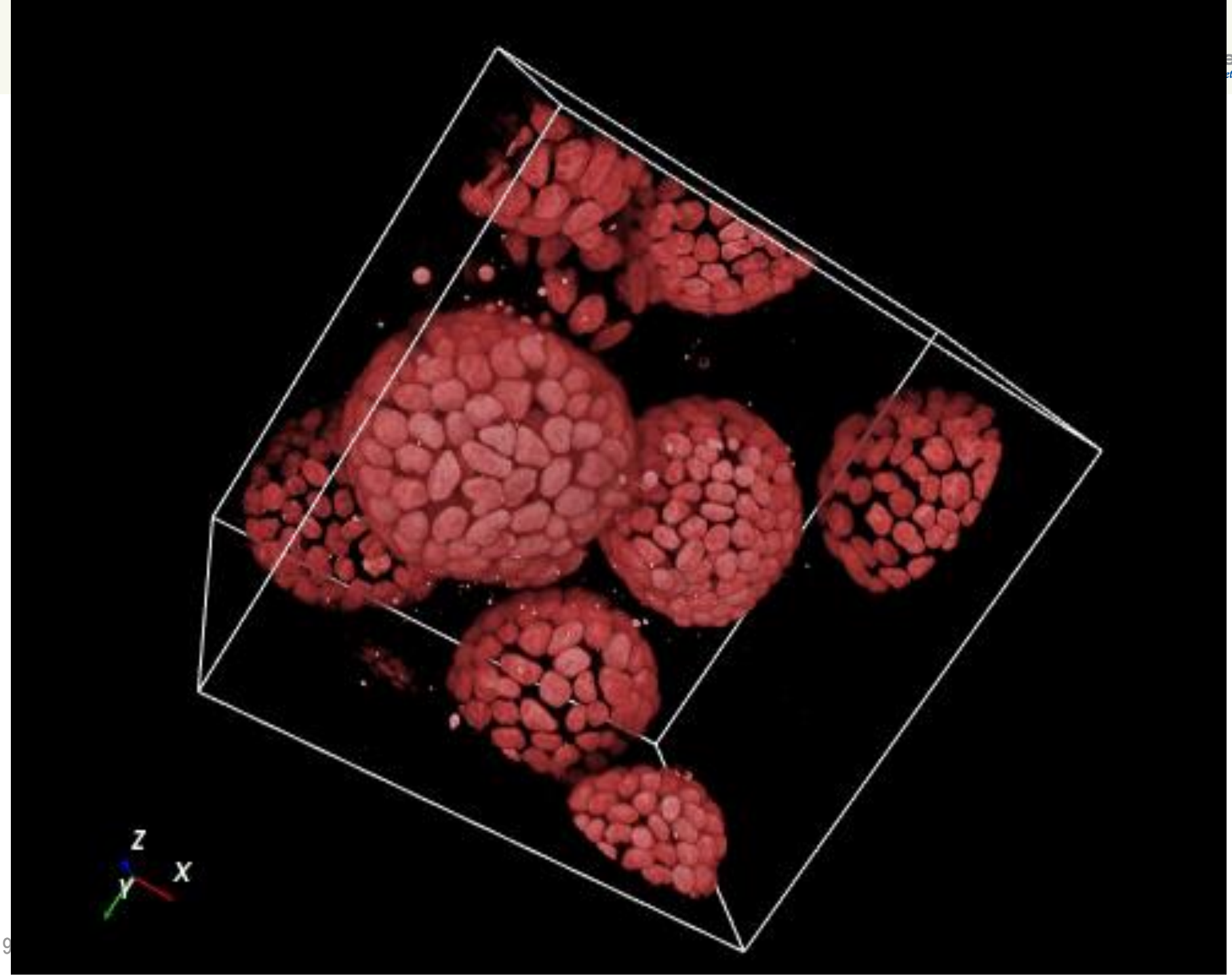
dsRED – Red Blood Cells



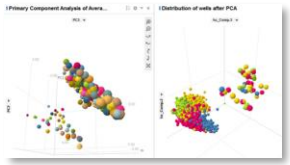

c. elegans brightfield

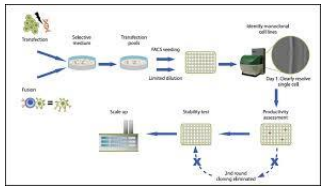


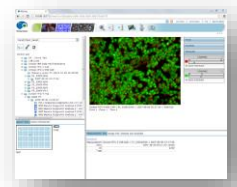
PerkinElmer
For the Better

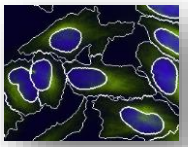

Z
X
Y

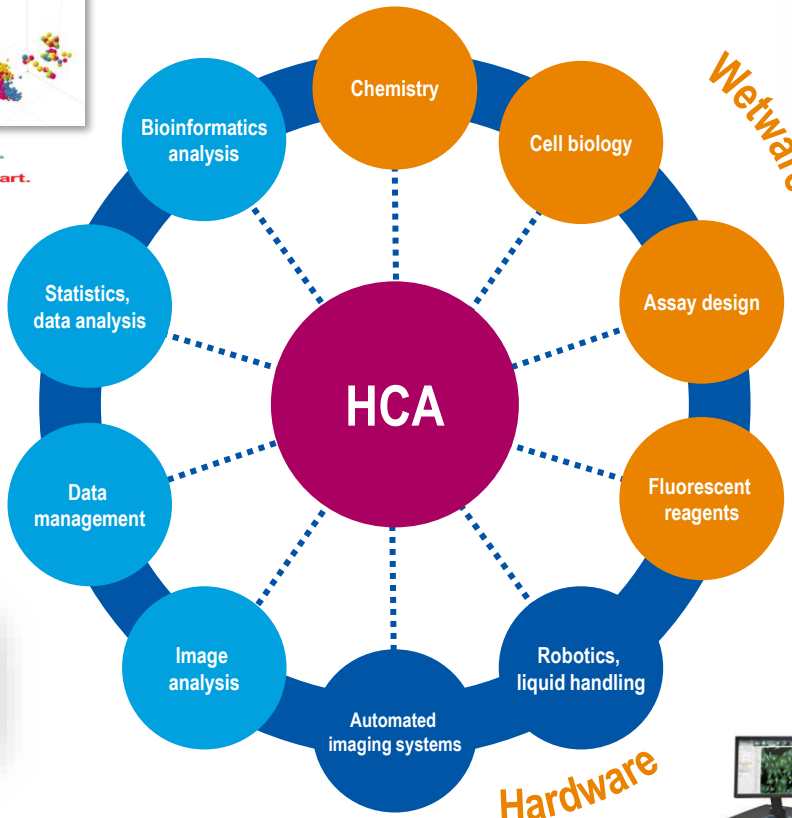
PerkinElmer提供HCS整体技术方案！从实验设计、硬件、到软件数据分析







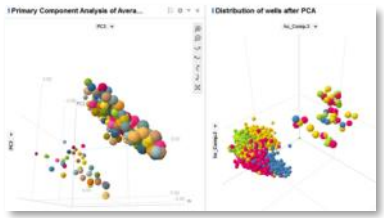




Adapted from Korn & Krausz,
Current Opinion in Chemical Biology 2007, 11:503–510

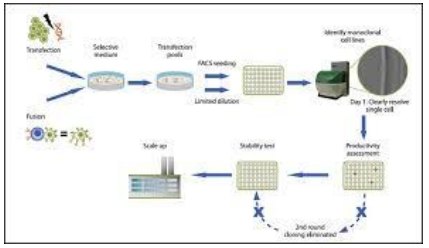
...is multi-disciplinary and challenging

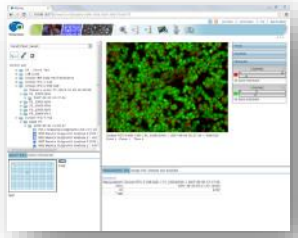
硬件优势



Spotfire
Easy. Fast. Smart.

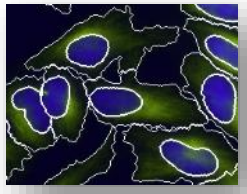
Wetware





Software

Columbus



Harmony

Bioinformatics analysis
Chemistry
Cell biology
Statistics, data analysis
Assay design
HCA
Data management
Fluorescent
Image analysis
Robotics, liquid handling
Automated imaging systems
Hardware

...is multi-disciplinary and

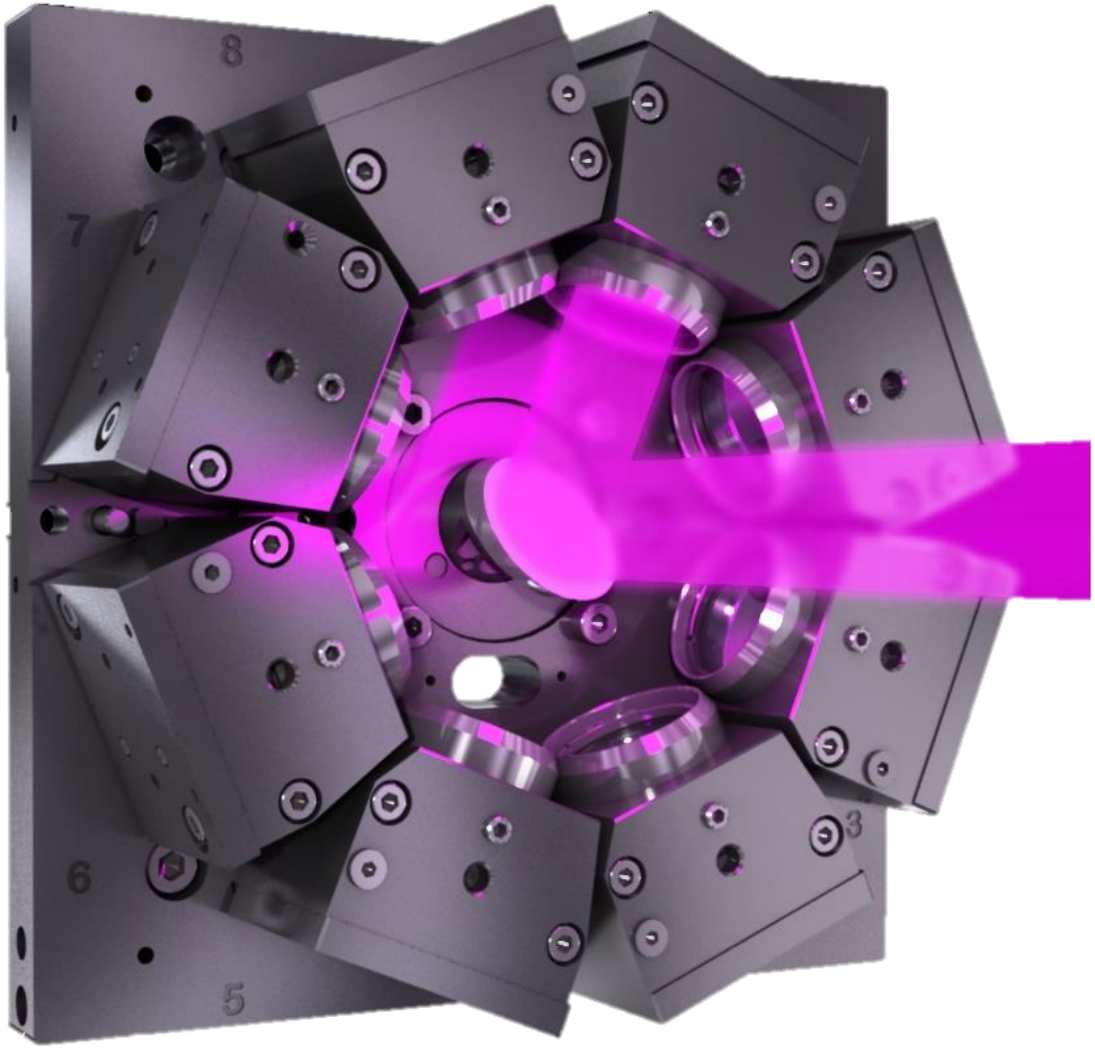
Adapted from Korn & Krausz,
Current Opinion in Chemical Biology 2007, 11:503–510

专业高内涵设计，避免外接部件

无需专业光路维护，无外漏光纤，无需暗室

Operetta CLS

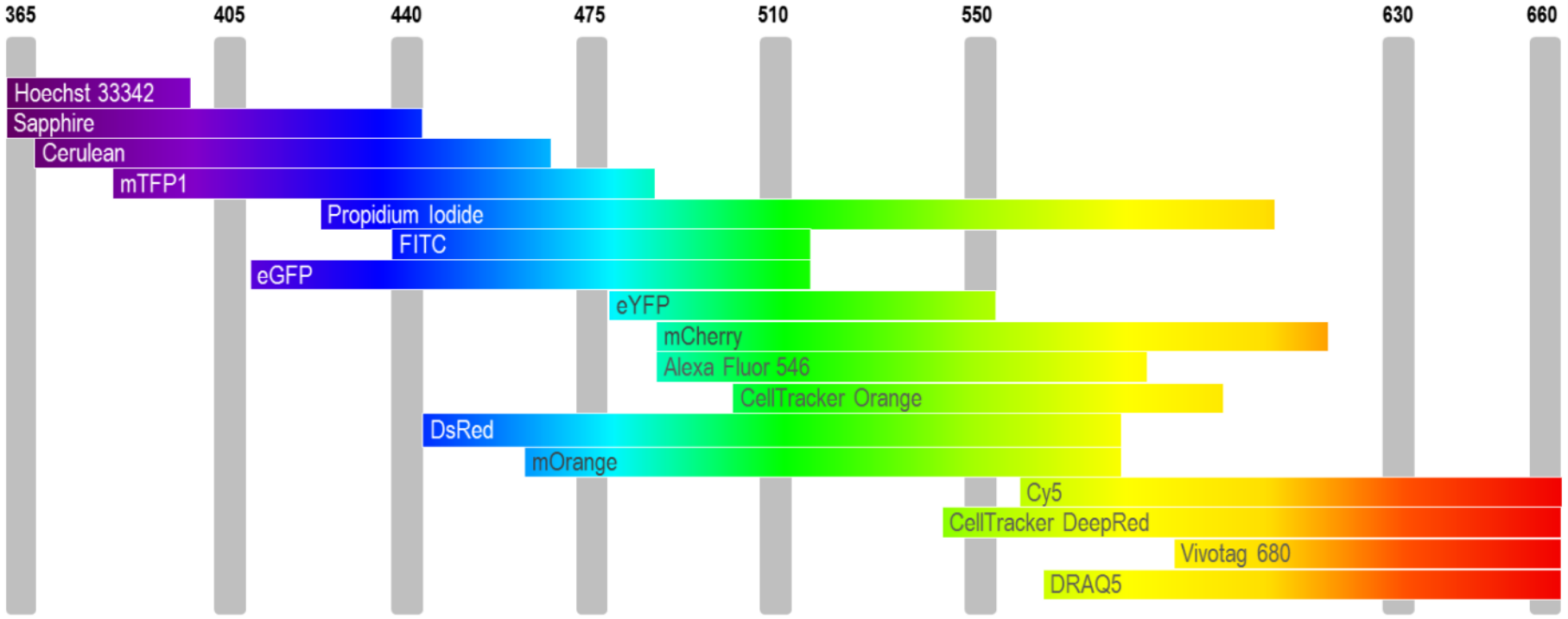
高能量LED光源



- 共聚焦专用高功率LED
- 免光纤设计，提高激发光能量

系统如何兼容更多染料

涵盖从UV 到NIR 广泛的激发谱线，适合多种应用需求

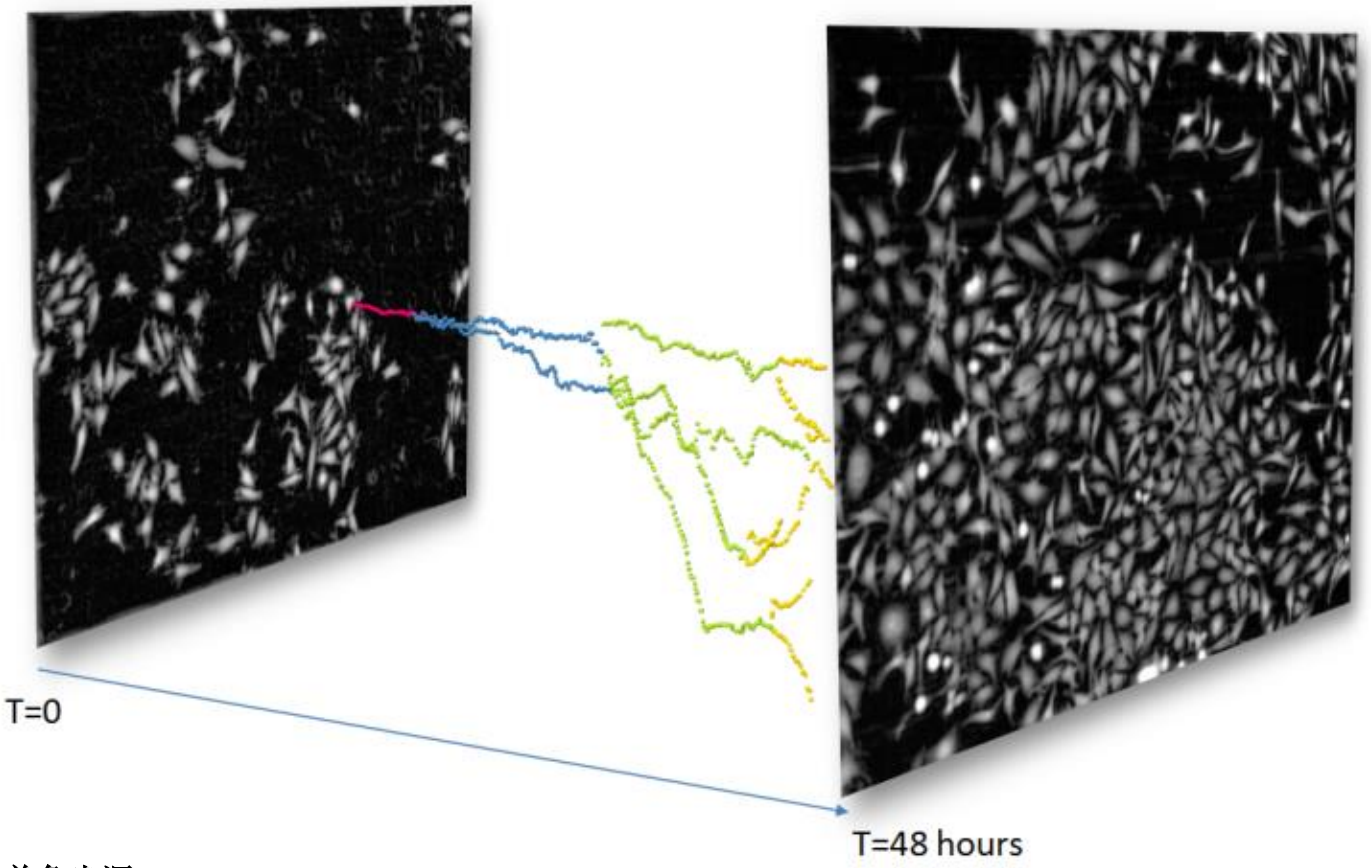


20x 0.4 N.A. Air Objective

20x 0.7 N.A. Water Objective

- 中高端市场唯一配备水镜的高内涵系统
- 透光量是普通空气镜的3~4倍

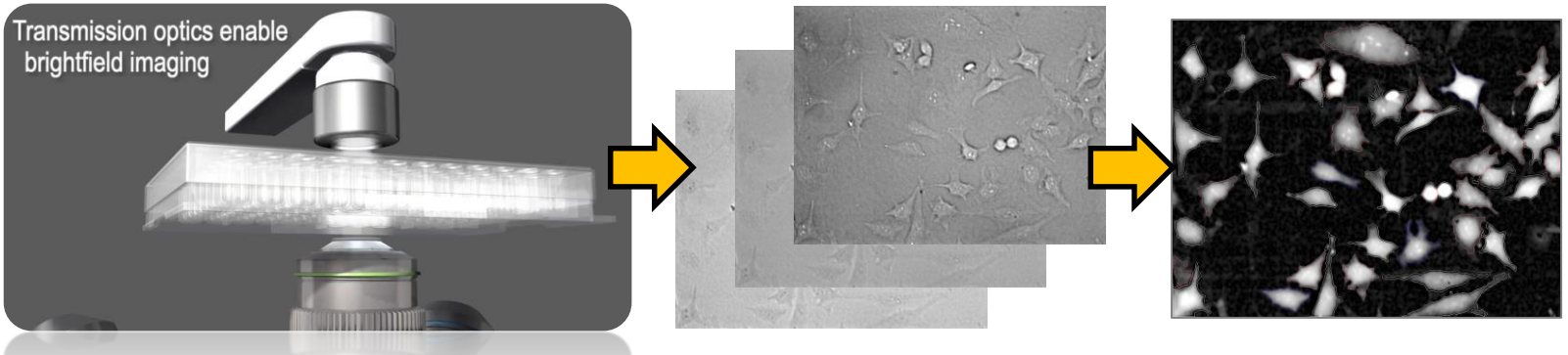
硬件优势：近红外单色LED，荧光级别高信噪比的非标记成像，实施无标记细胞检测



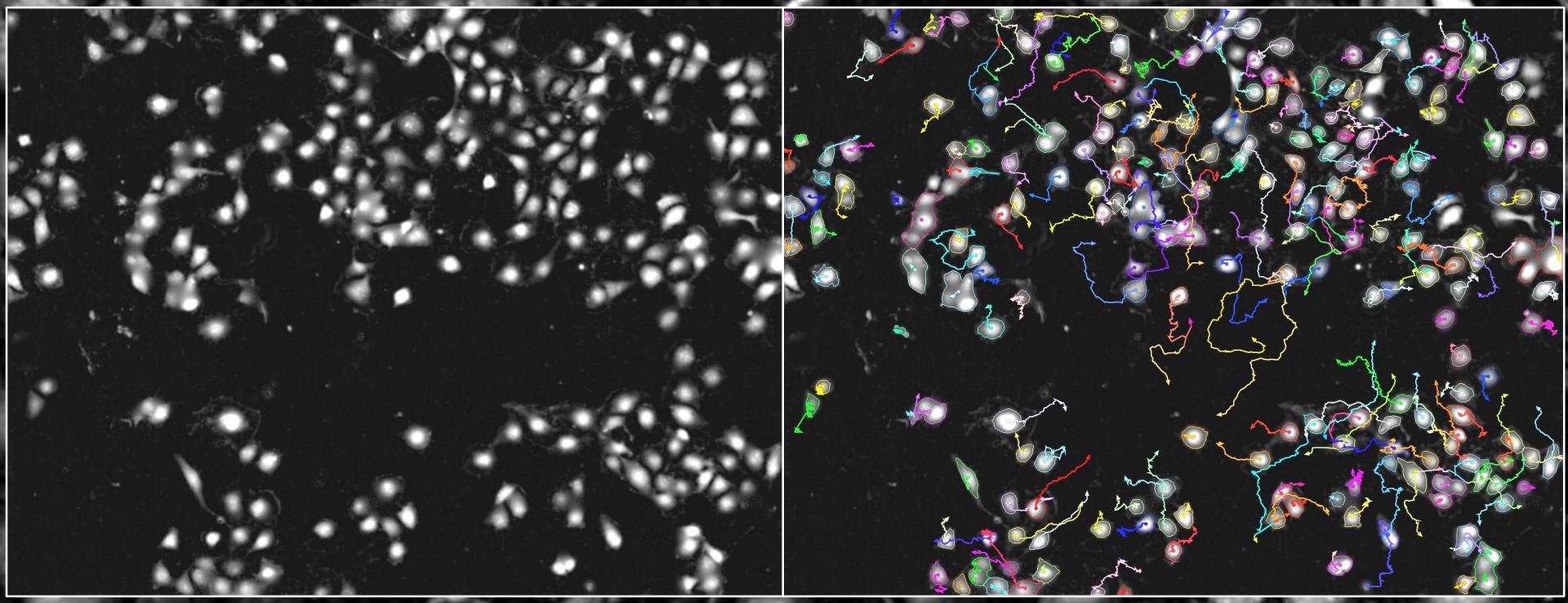
单色光源

焦距包围成像

数字转换



南京大学：DPC模式下的细胞分裂和运动轨迹追踪



硬件优势：长时间活细胞在线观察实验—— 5天在线培养

nature COMMUNICATIONS

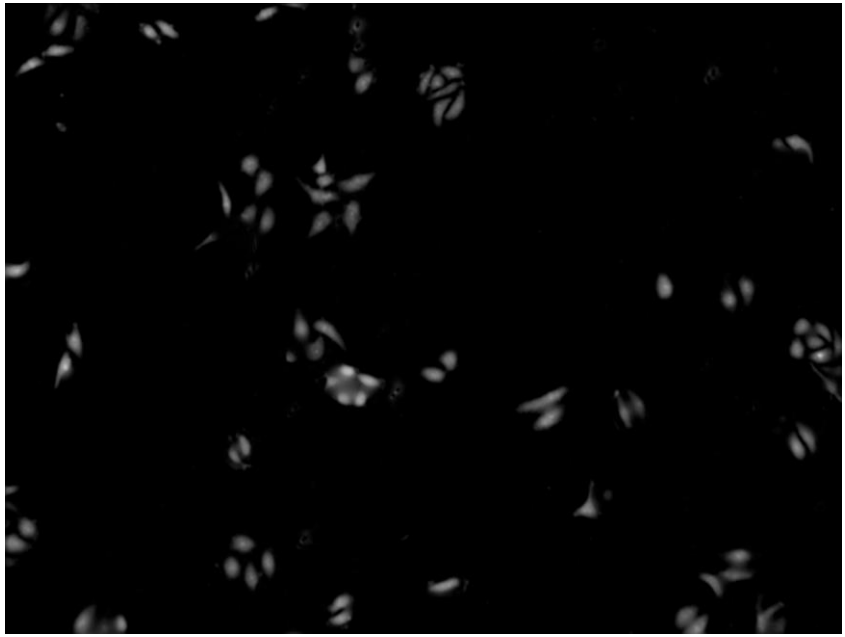
ARTICLE

Received 13 Jul 2013 | Accepted 2 Jan 2014 | Published 27 Jan 2014

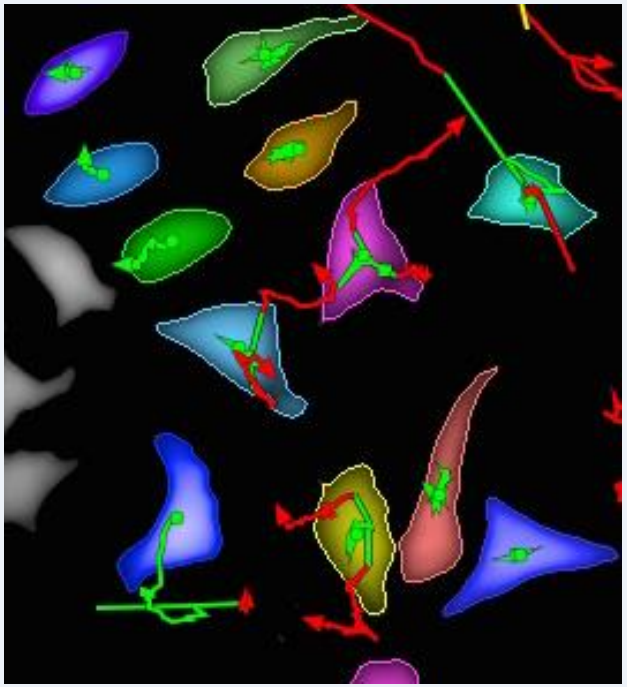
DOI: 10.1038/ncomms4195 OPEN

Clonal culturing of human embryonic stem cells on laminin-521/E-cadherin matrix in defined and xeno-free environment

a cell incubator. After that, the plates were transferred into a high throughput imaging system (Operetta PerkinElmer) equipped with an environmental control unit (37 °C, 5% CO_2). For Supplementary Movies 1 and 2, the brightfield images were taken once in 15 min during 24 h after plating using Harmony software (PerkinElmer), exported and analysed using ImageJ software (NIH, the United States). For Supplementary Movie 3, the images were taken once in 30 min for 5 days. For migration



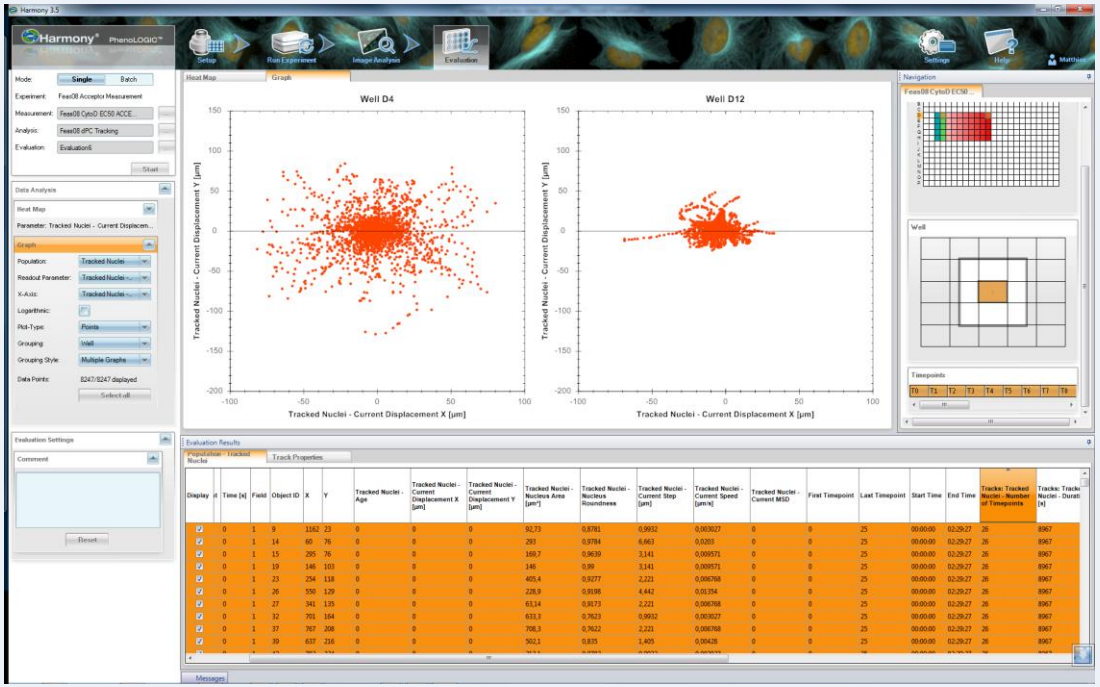
无标记迁移、代次分析



Tracking of dividing cells on a digital phase contrast image

Green: Track of first generation

Red: Second generation

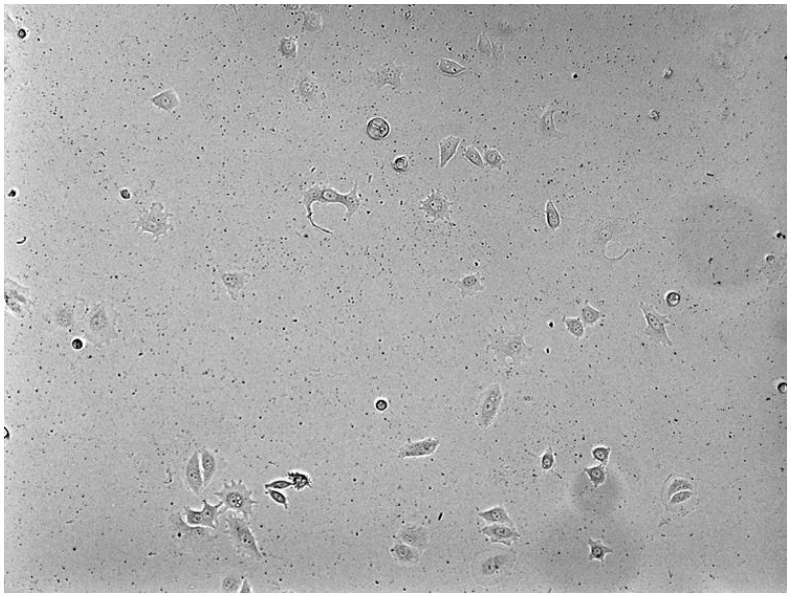


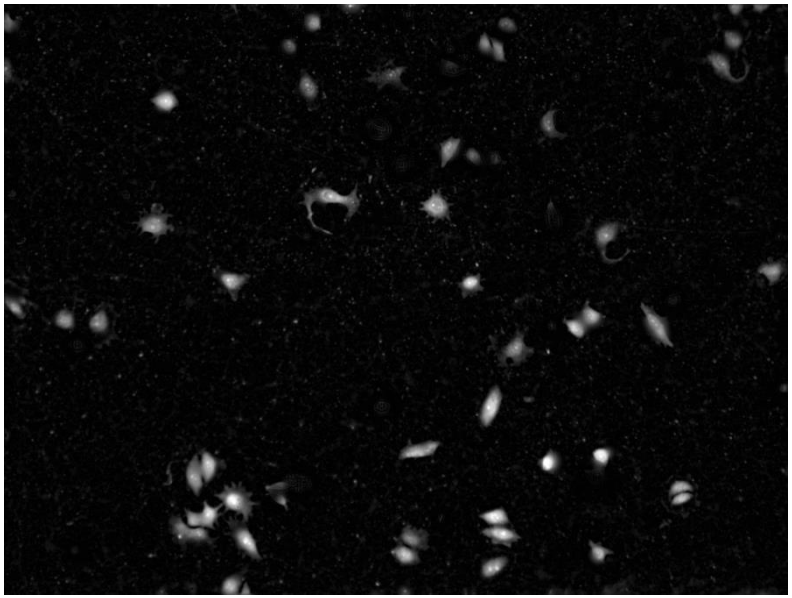
untreated

treated

Longitudinal cell studies to quantify dynamic behavior

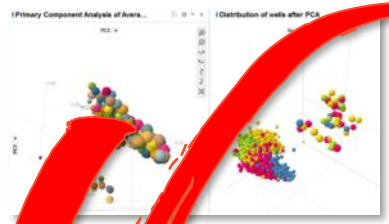
DPC 非标记应用——非标记方式获取高信噪比细胞类荧光图像





- 细胞计数
- 细胞形态分析
- 细胞迁移能力分析
- 细胞世代分析
- 神经细胞分析
- 克隆形成
- 微组织形态学分析
- 细胞浆/膜蛋白表达分析

高内涵分析平台建设



Spotfire
Easy. Fast. Smart.

Columbus

Harmony

Software

Wetware

Hardware

CA

Bioinformatics analysis

Chemistry

Cell biology

Assay design

Fluorescent reagents

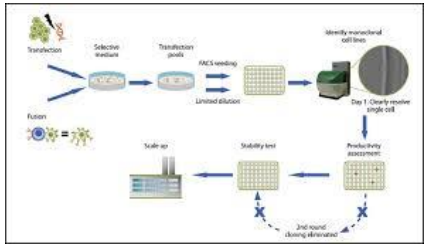
Robotics, liquid handling

Automated imaging systems

Image analysis

Data management

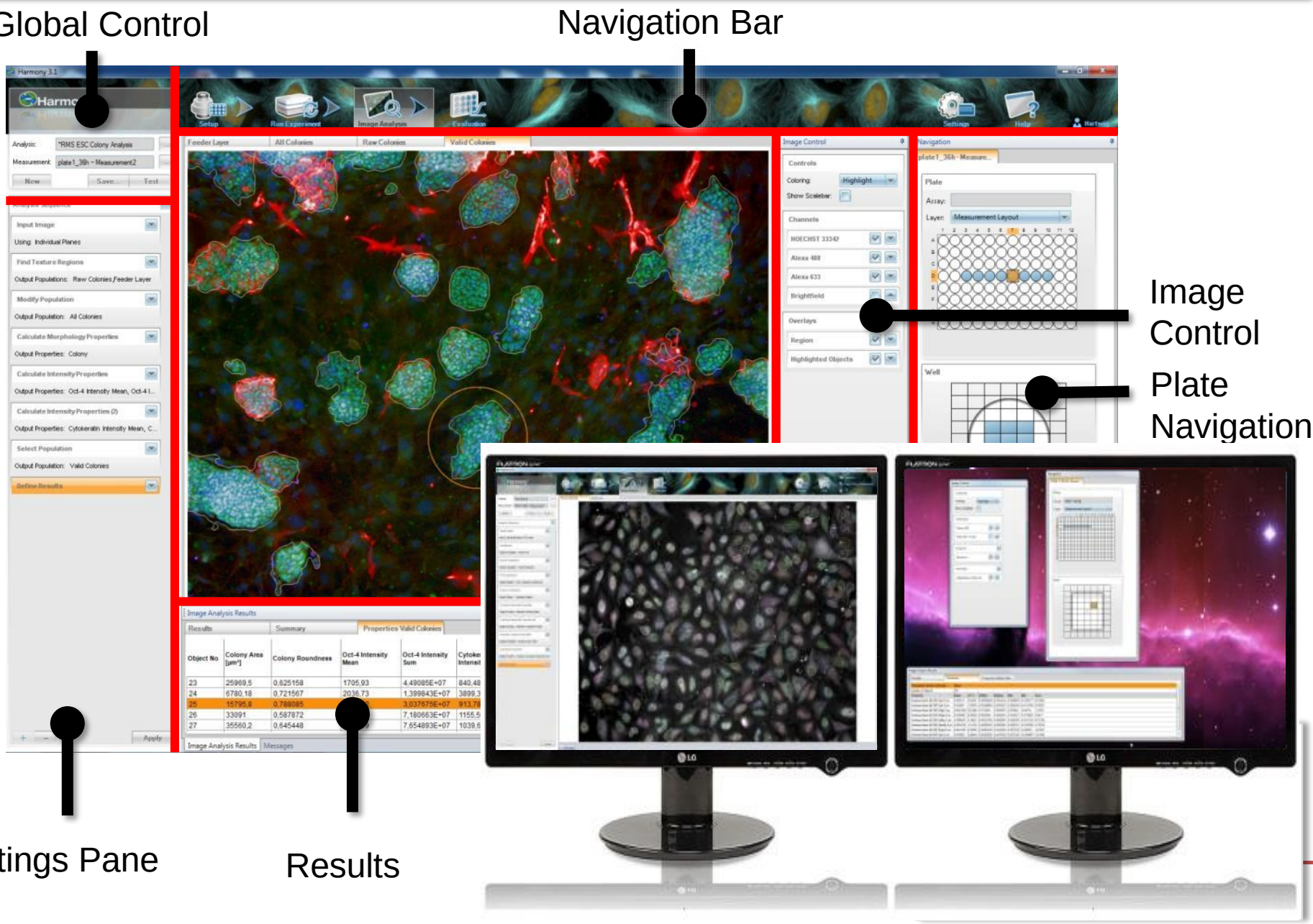
Statistics, data analysis



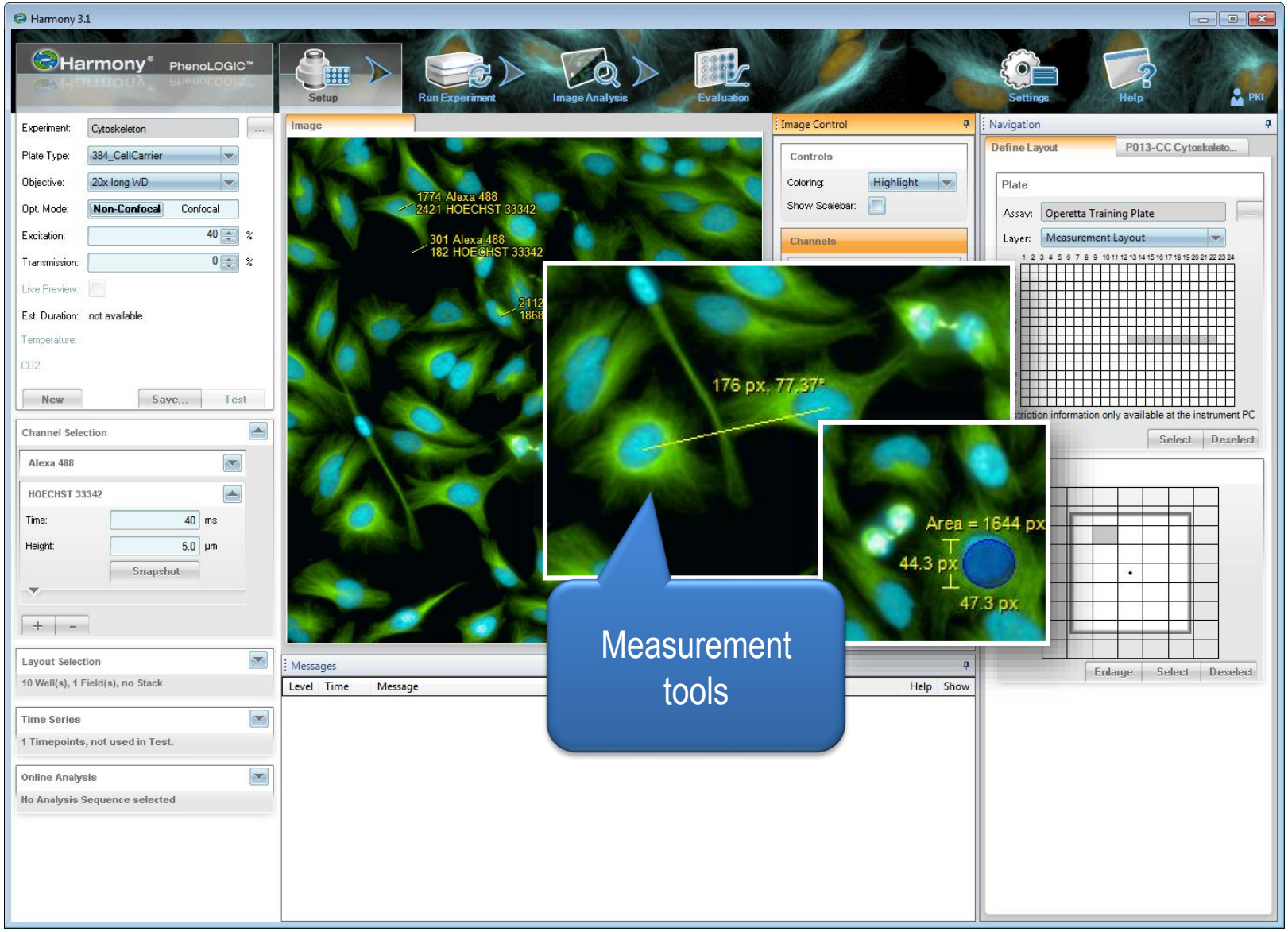
...is multi-disciplinary and challengin

Adapted from Korn & Krausz,
Current Opinion in Chemical Biology 2007, 11:503–510

软件优势：简介的界面和流程设计，让使用越来越简单



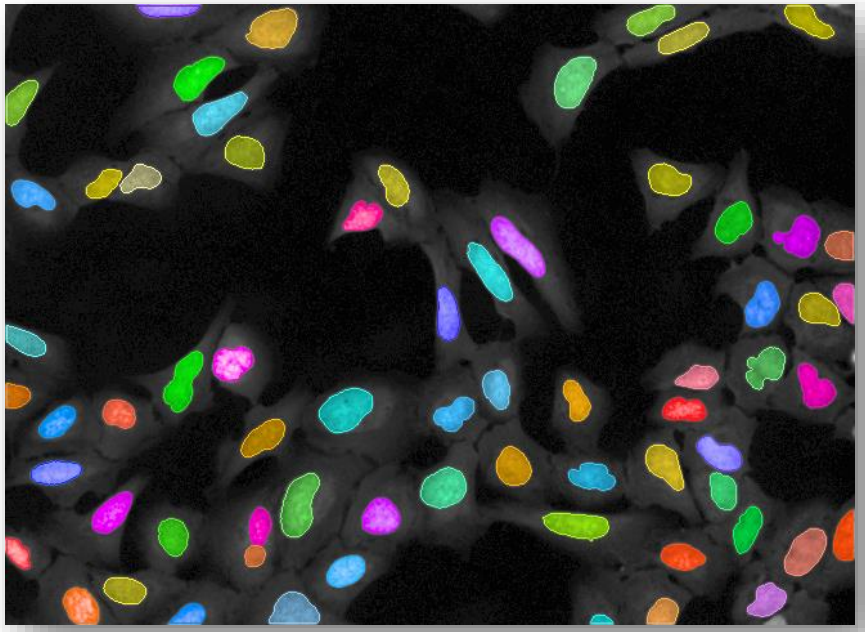
软件优势： Image View Tools 图像查看功能



Show intensities, measure

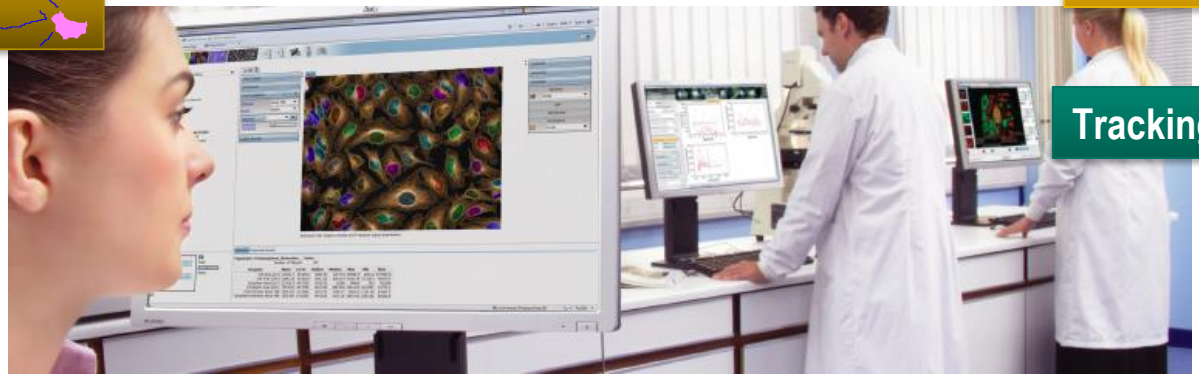
图像分析的分析模块 building blocks

- Find Nuclei
- Find Cells
- Find Cytoplasm
- Find Spots
- Find Micronuclei
- Find Texture Regions
- Find Image Regions
- Find Neurites



- Calc. Intensity
- Calc. Morphology
- Calc. Texture
- Calc. Properties a^2+b

- Select Cell Region
- Select Region
- Select Population



Tracking object

一键化操作的细胞检测—— 15步 VS 1 步

传统软件选择细胞核，必须先填写最大细胞核，最小细胞核直径尺寸，测量背景数值，测量细胞数值，细胞减去背景。。。

4. Move the cursor to the opposite edge of the object and note the Length value.

5039429 B

Configuring Application Modules

In the following example, the value is 10 pixels (or 12.87 µm). This number represents the cell width in pixels. If the image is calibrated, then the length is in pixels and calibrated units.

2. Select the **Arrow** tool as shown in the following figure.

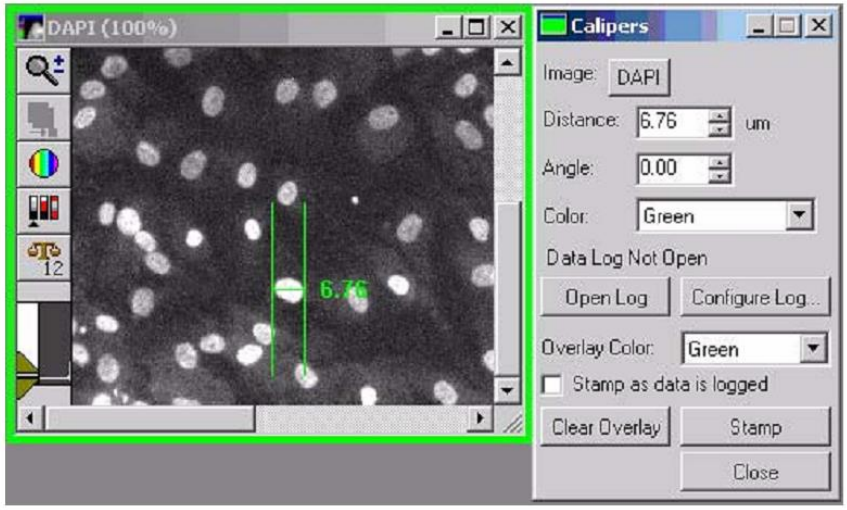
3. Move the arrow cursor over the dimmest part of the dimmest object in the image.

As you move the cursor, the X,Y coordinates and the gray-level value of the pixel under the cursor are indicated at the bottom of the MetaXpress Software desktop. The X,Y coordinates are in parentheses and the gray-level value is to the right of the arrow. For example:

(101, 80) -> 366

4. Note the gray-level value of the object.

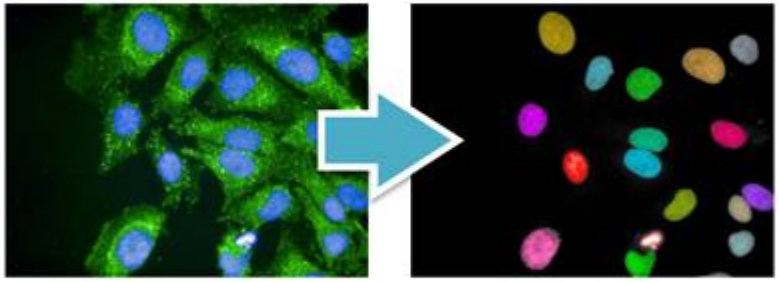
5. Move the cursor just outside the object to the background of the



gure 7-6 Calipers Sample Image and dialog box

PE Harmony

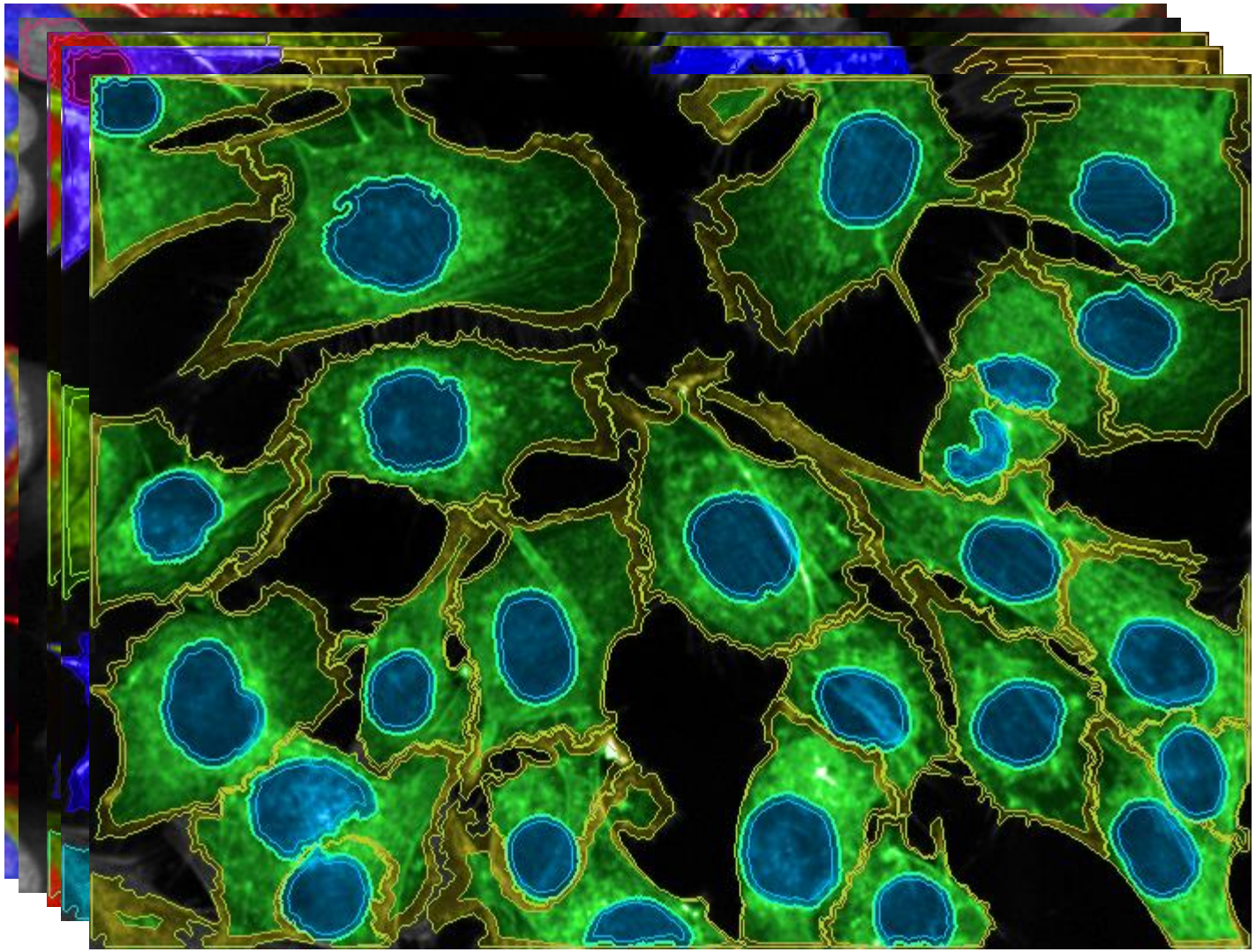
Step 1. Find Nuclei is good enough for getting the numbers.



Summary | Properties Nuclei

Property	Mean	CV %	StdDev	Median	Max	Min	Sum
Area [µm²]	266.571	34.539	92.071	249.36	440.55	86.4	4531.71
Area [px²]	9728.12	34.5385	3359.94	9100	16077	3153	165378
Intensity DRAQ5	1739.34	19.949	346.98	1650.77	2977.42	1395.94	29568.7
Contrast DRAQ5	0.426285	14.5611	0.0620718	0.415631	0.649076	0.354963	7.24685

怎么完成细胞的高内涵分析？



Image

⇩

Find nuclei

⇩

Find cytoplasm

⇩

Segmentation

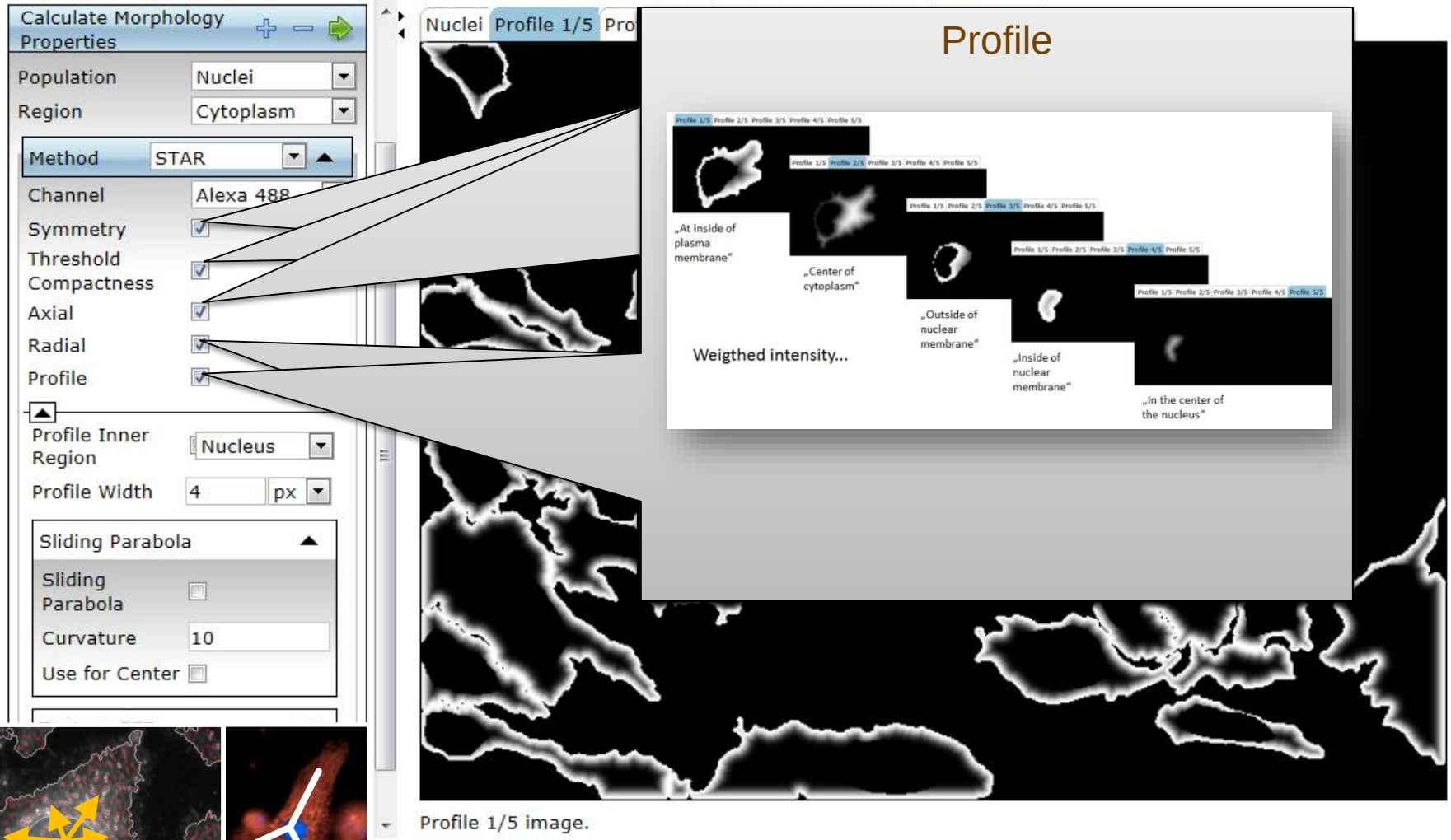
⇩

Content analysis

⇩

Quantity

专为高内涵海量细胞分析设计的 STAR 整特征分析

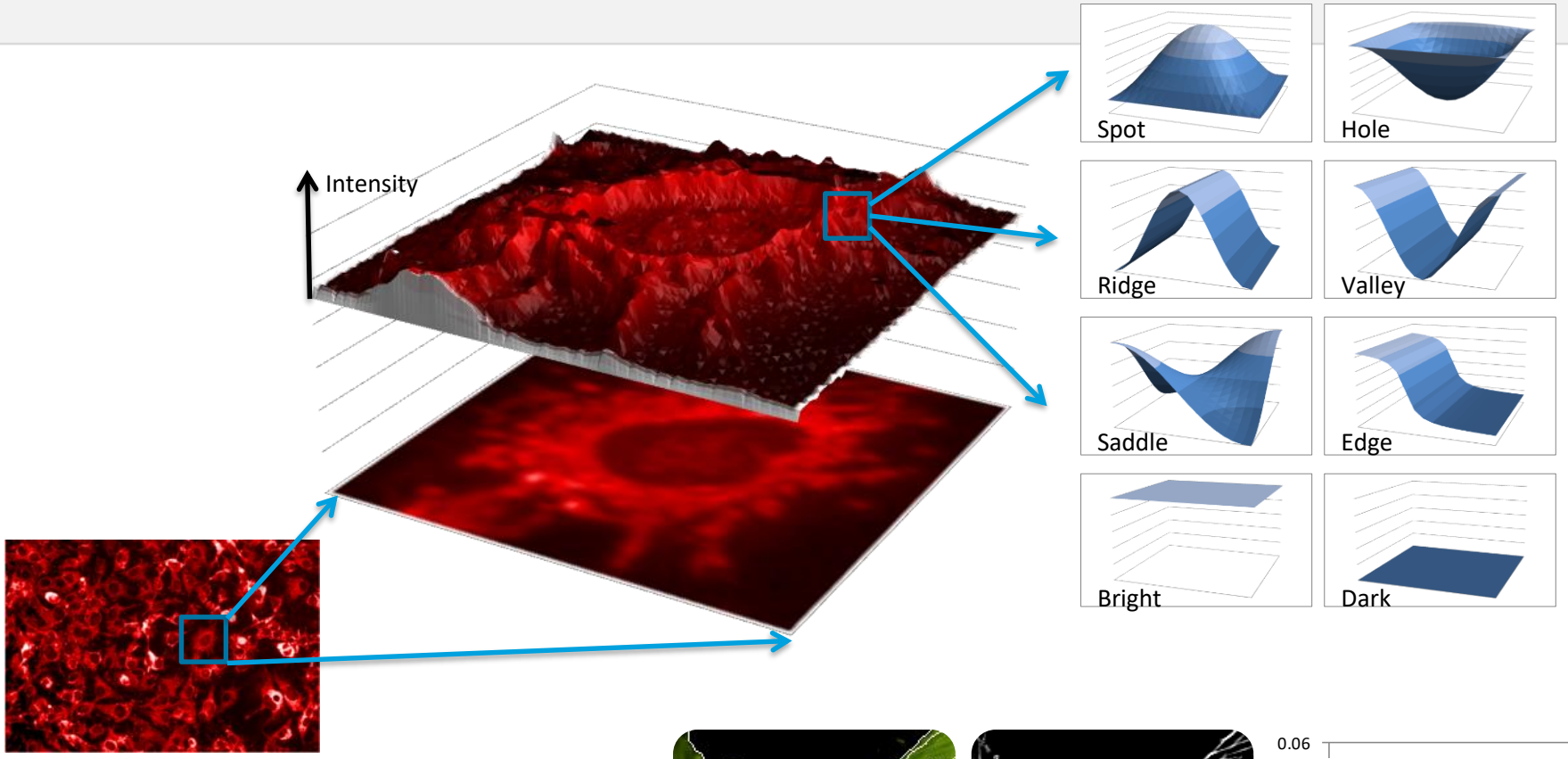


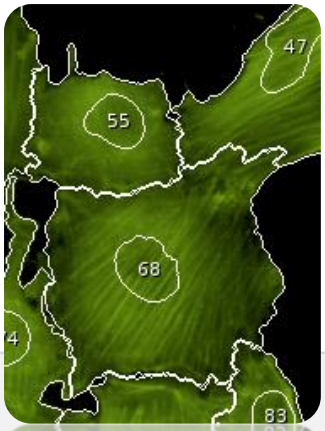
STAR = Symmetry（对称性）, Threshold Compactness（信号密度）, Axial（轴向）, Radial（放射性）

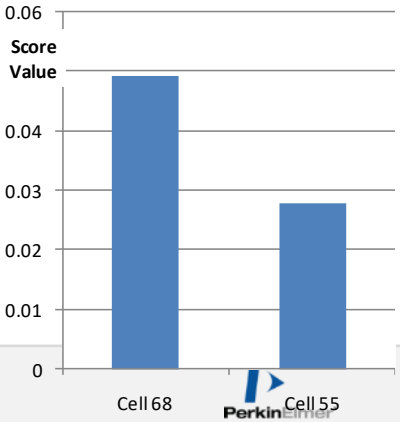
Profile: 亚细胞分区

识别越来越精准！

纹理分析——量化“看上去不一样”的细胞



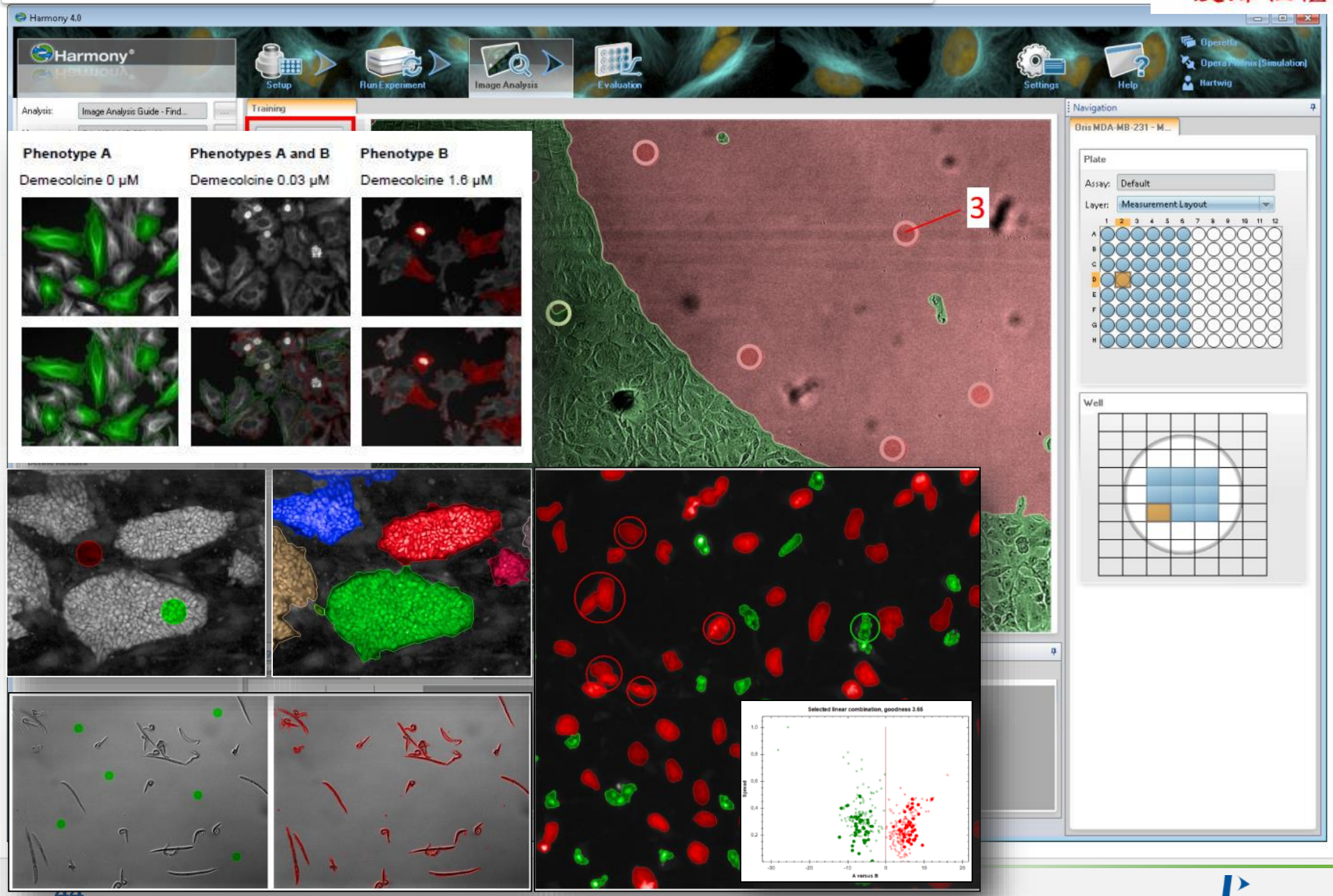




对比越来越显著！

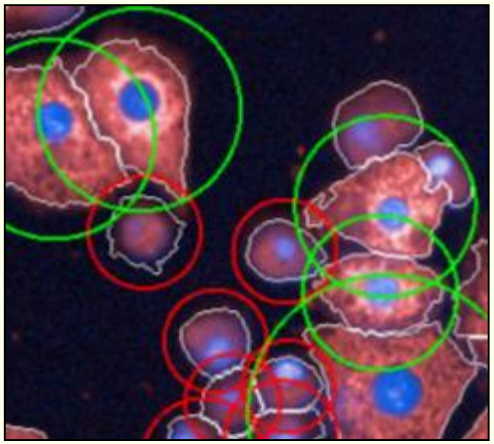
Source: Operetta™ Application Guide

软件优势：软件自学习，轻松分组样品，不仅仅是细胞分类

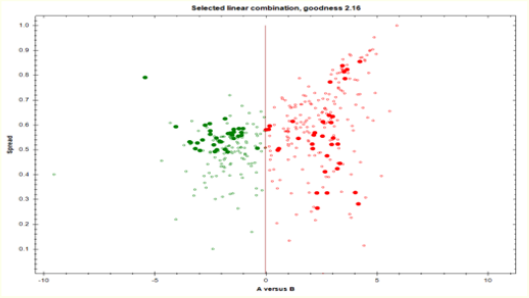


细胞纹理自学习——转化观察经验为软件语言

Train on dead cells

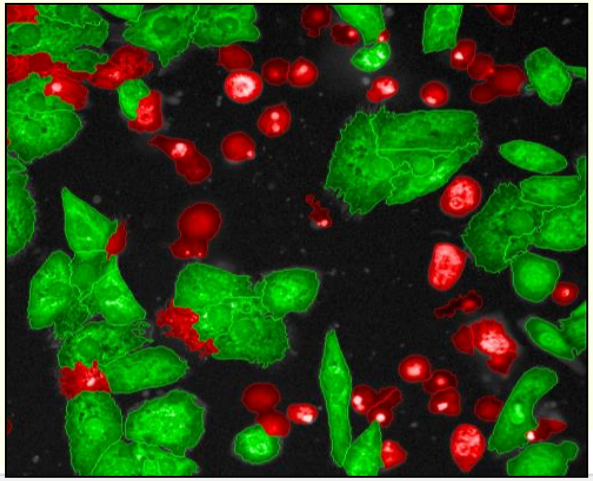


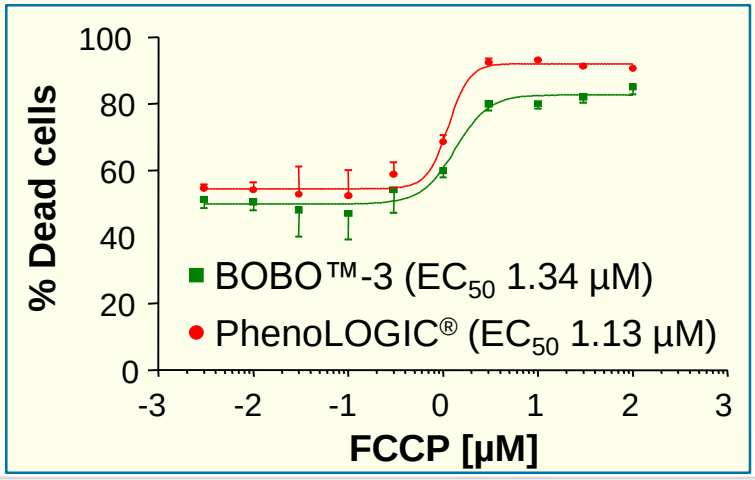
PhenoLOGIC



4 out of 29 properties used to calculate a classifier

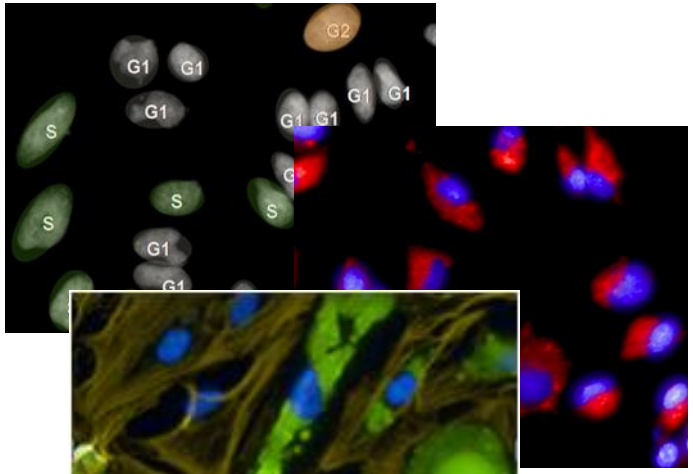
Classification result

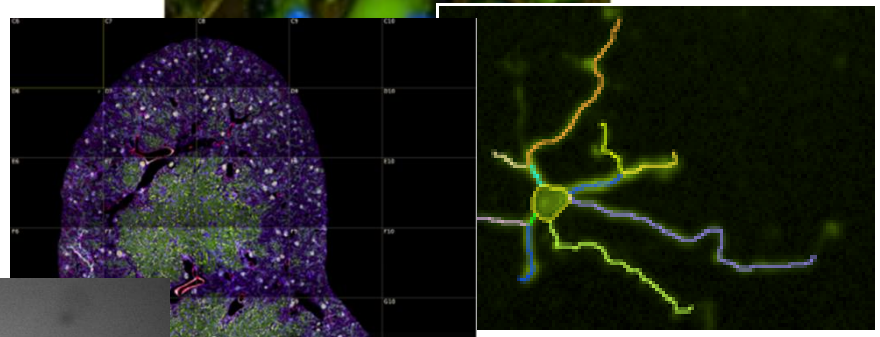


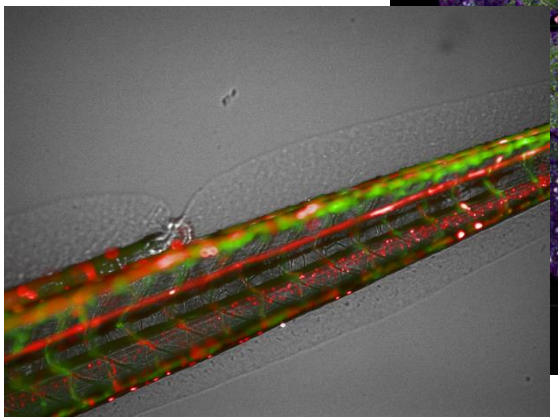


适用研究方向

- 肿瘤研究 (细胞周期、细胞增殖与凋亡、细胞迁移等分析)
- 炎症研究 （GPCR、信号通路研究）
- 心血管疾病研究（动脉硬化分析）
- 中枢神经及疼痛研究（神经元分析）
- 靶点验证（RNA干扰分析）
- 病毒研究（病毒滴度测定，抗病毒药物筛选等）
- 干细胞及分化研究
- 药物筛选

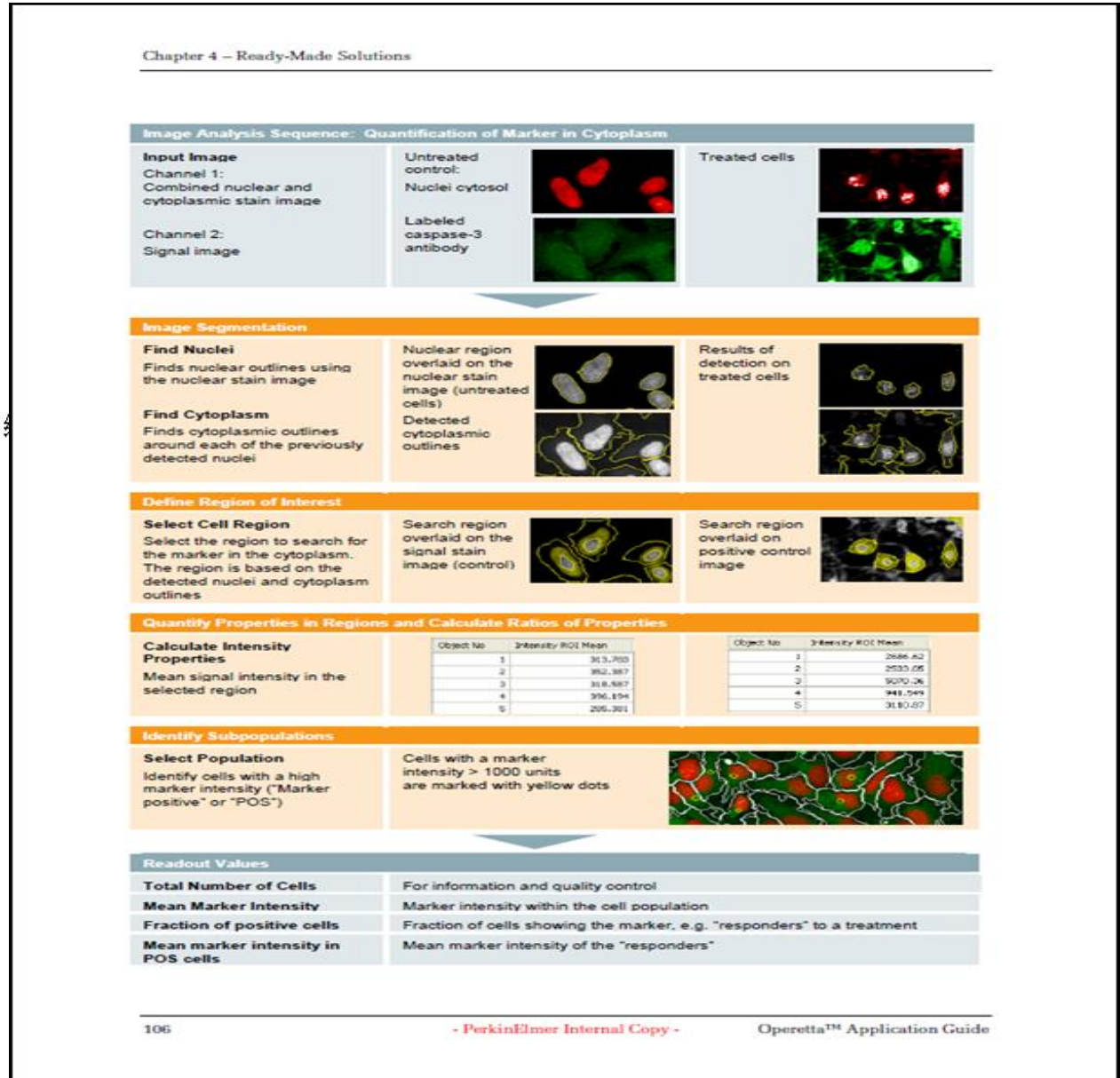






39种预制分析方案

- 蛋白表达量分析
- 细胞形态学分析
- 核质转位
- 细胞凋亡
- 细胞周期分析
- 细胞毒性分析
- 细胞迁移
- 细胞自噬
- 干细胞克隆分析
- 无标记代次分析
- 神经细胞神经元检测
- 3D MicroTissue



Chapter 4 – Ready-Made Solutions

Image Analysis Sequence: Quantification of Marker in Cytoplasm

Input Image
Channel 1:
Combined nuclear and cytoplasmic stain image

Channel 2:
Signal image

Untreated control:
Nuclei cytosol

Labeled caspase-3 antibody

Treated cells

Image Segmentation

Find Nuclei
Finds nuclear outlines using the nuclear stain image

Find Cytoplasm
Finds cytoplasmic outlines around each of the previously detected nuclei

Nuclear region overlaid on the nuclear stain image (untreated cells)

Detected cytoplasmic outlines

Results of detection on treated cells

Define Region of Interest

Select Cell Region
Select the region to search for the marker in the cytoplasm. The region is based on the detected nuclei and cytoplasm outlines

Search region overlaid on the signal stain image (control)

Search region overlaid on positive control image

Quantify Properties in Regions and Calculate Ratios of Properties

Calculate Intensity Properties
Mean signal intensity in the selected region

Object No	Intensity ROI Mean
1	313.703
2	352.387
3	318.587
4	396.154
5	295.391

Object No	Intensity ROI Mean
1	2686.42
2	2533.06
3	3070.26
4	941.549
5	3180.87

Identify Subpopulations

Select Population
Identify cells with a high marker intensity ("Marker positive" or "POS")

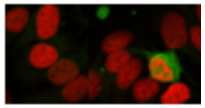
Cells with a marker intensity > 1000 units are marked with yellow dots

Readout Values

Total Number of Cells	For information and quality control
Mean Marker Intensity	Marker intensity within the cell population
Fraction of positive cells	Fraction of cells showing the marker, e.g. "responders" to a treatment
Mean marker intensity in POS cells	Mean marker intensity of the "responders"

106 - PerkinElmer Internal Copy - Operetta™ Application Guide

Ready-Made



166

Figure 5-1: Schematic repr
fragmentation and caspase-

5.1.1 Introdu

There are two main pa
mediated pathway, an
finally result in the ac
which are considered
Shi Y; Hengartner MC

We describe a high-co
experimentally trigger
staurosporine[1] (see gl
activated caspase-3, a
addition, we evaluate
as well as the fragmen

5.1.2 Materi

CellCarrier 384-well (
bioone # 676090); Hel
#72400) + 10% FBS (S
H15-002); Hoechst333
Serum (Sigma #9023);
Antibody, Alexa Fluo

6E3 ca

	1	2	3
A			
B			
C			
D			
E			
F			
G			QuM
H			
I			
J			
K			
L			
M			
N			
O			
P			

Figure 5-2: Plate layo

Image Acquisitio

- Use the 2
- Open the
- Load the sequence Alexa 48 as describ
- Adapt the samples (
- Switch to
- Optional:
- **Run** the a

Dye	Ex./ Max.
DRAQ5™ (nucleus/ cytoplasm, specific stain for nucleic acids)	647 /
Cleaved-caspase-3 antibody (Alexa Fluor® 488 conjugate)	494 /

Table 5-1: Fluorescence cha

Image Analysis

- Load the analys
- Select the **Find** nuclei detectio general descrip special hints o fragments are d
- Adjust the thre **Population** bui Marker" (4.6) f

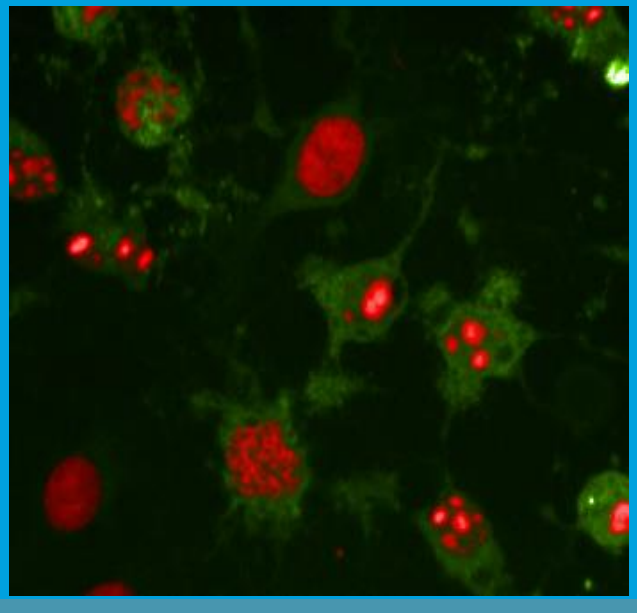
The ready-made analy
building blocks:

Image Analysis: RMA Apoptosis 1		
Input Images	DRAQ5™ nuclear stain channel	Alexa 488 Caspase-3 channel
Image Segmentation		
Find Nuclei	Detects Nuclei in the DRAQ5 channel	
Definitions of Regions of Interest		
Select Cell Region	Define an enlarged region of interest (ROI) in the DRAQ5 channel by setting the outer border of the nuclear region to - 80 % and the inner border to 100 % (see section 4.11.3). With this region (**MarkerROI**) we will later quantify the intensity of the Alexa 488 detection channel.	
Select Region	Define a shrunken selection of the nuclei (**NucFragROI**) by scaling down the outer border about 2 pixels (px)	
Quantifying Properties in Regions		
Calculate Intensity Properties	Use the **MarkerROI** to quantify properties of the marker channel (caspase-3): - Mean Intensity of the marker - Standard Deviation of the marker - Median Intensity of the marker	
Calculate Intensity Properties (2)	Quantify the properties of the nucleus, using **NucFragROI** as a region in the nuclear channel: - Coefficient of Variance (CV) Intensity - Sum Intensity	
Calculate Morphology Properties	Quantify the properties of the nucleus, using the standard Nuclear region: - Area of a nucleus	
Select Subpopulation		
Select Population	Apply a threshold to find a population which has a high mean marker intensity (to be adjusted). This population is defined as apoptotic cells.	
Calculate Readout Values		
Define Results	Select and calculate values to report back as the results for each well	

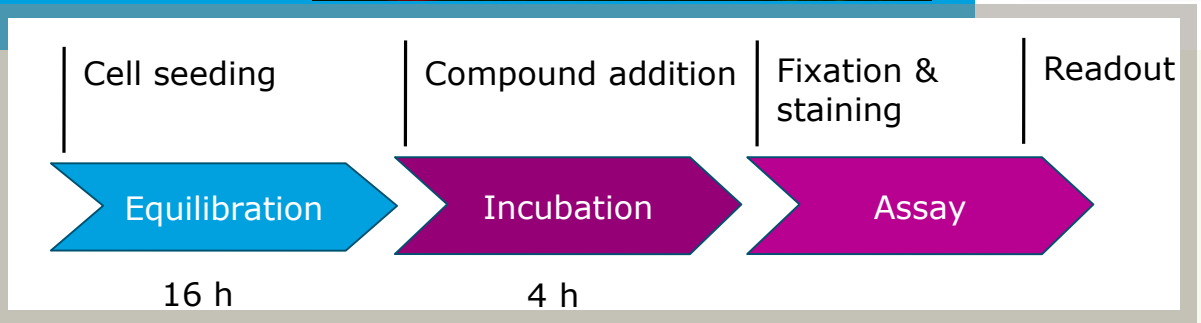
PerkinElmer

PerkinElmer
For the Better

HUMAN HEALTH | ENVIRONMENTAL HEALTH



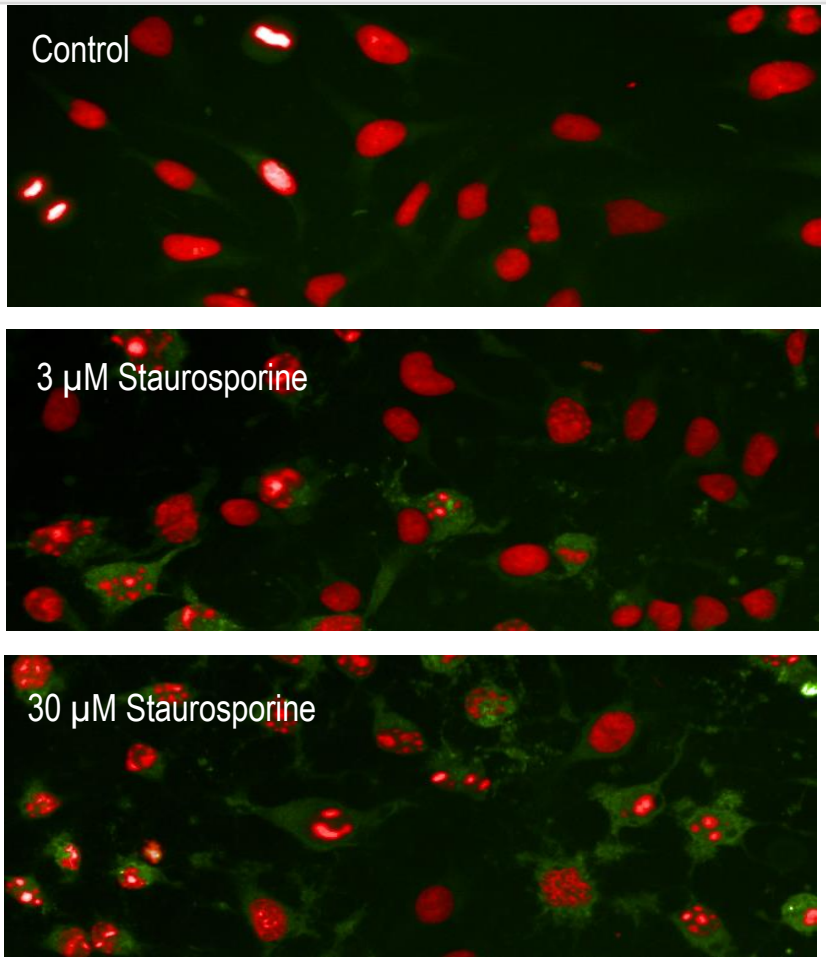
细胞凋亡研究



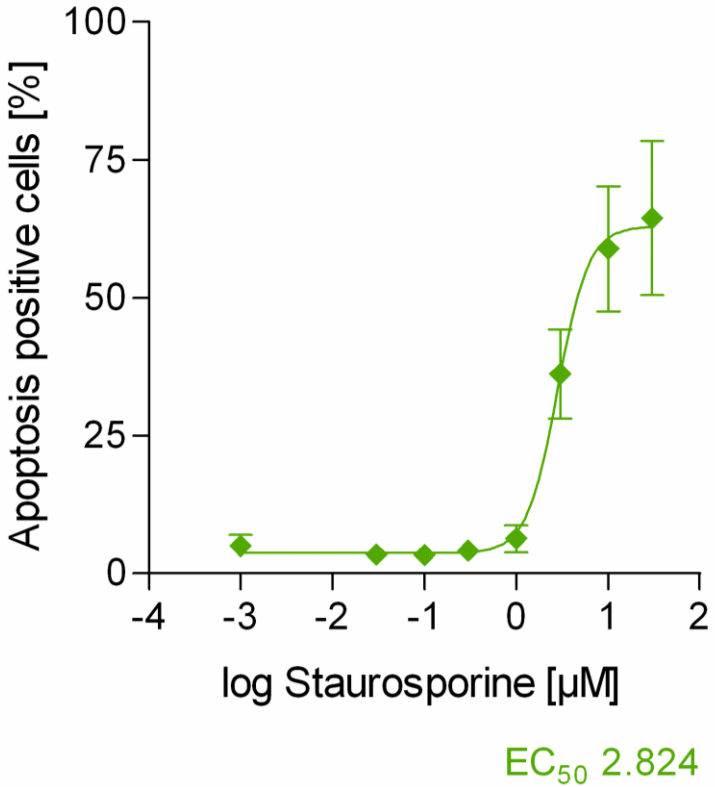
凋亡检测 – 成像

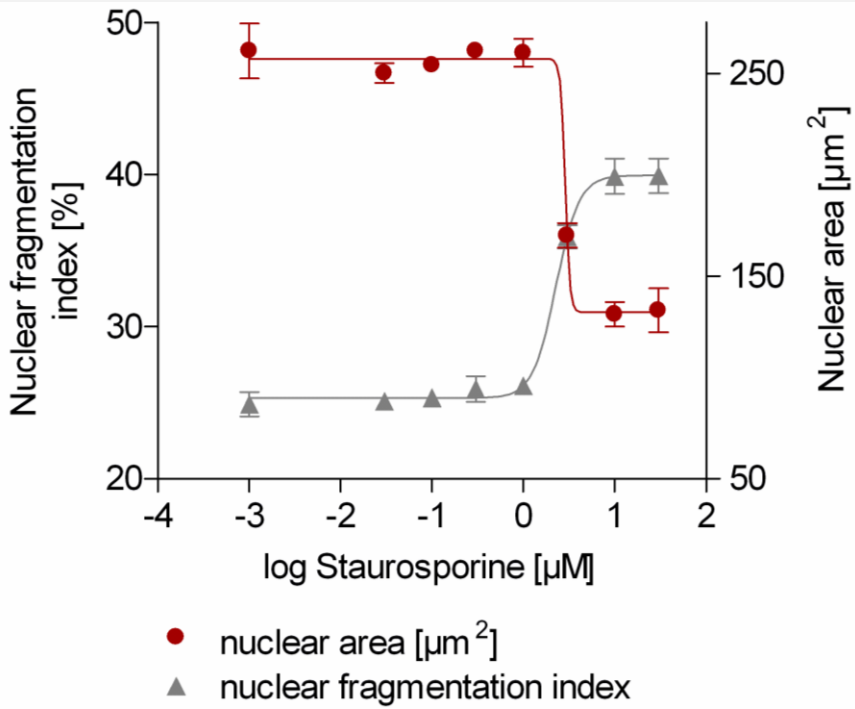
Caspase 3 活化	Alexa Fluor® 488 labeled anti caspase-3 antibody
细胞计数	DRAQ5™
细胞核大小	DRAQ5™
细胞核碎片化	DRAQ5™

- 20x long WD 物镜成像
- 增加十字胞碱浓度导致caspase-3增加
- 药物处理后的细胞核表现出典型的凋亡现象，核皱缩，面积变小，亮度增加；在凋亡晚期细胞核碎片化



凋亡检测—结果





- Caspase-3 based readout (left) and nuclear morphology based readout (right) show **similar EC_{50} values** for staurosporine.

a. 样本制备简单，检测通量高。不需要消化细胞的过程，可以批量对96或者384个样本进行处理制备，批量对样本进行数据读取。

b. 单次实验获得的实验结果内容丰富，不仅有凋亡标志蛋白的定量检测，还可以同时分析细胞核的形态学变化。

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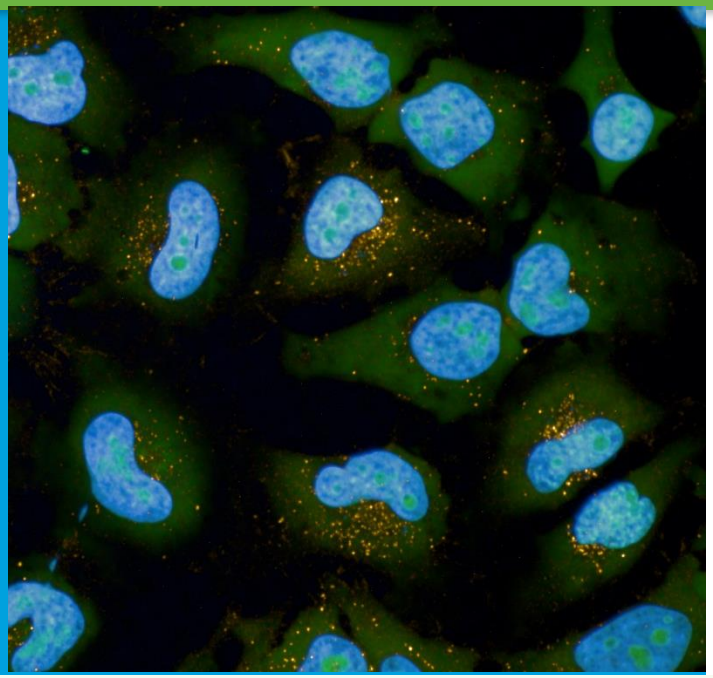
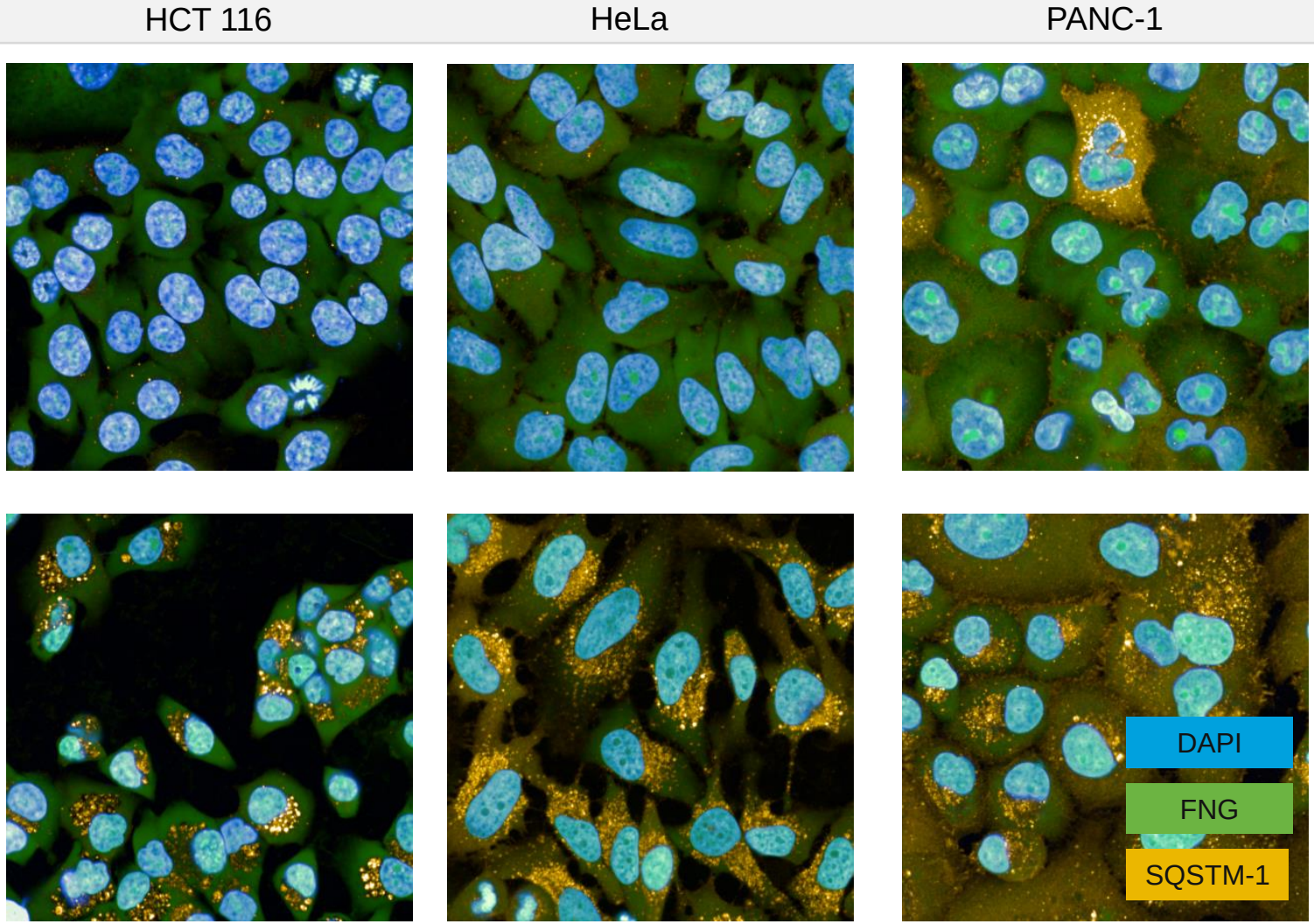


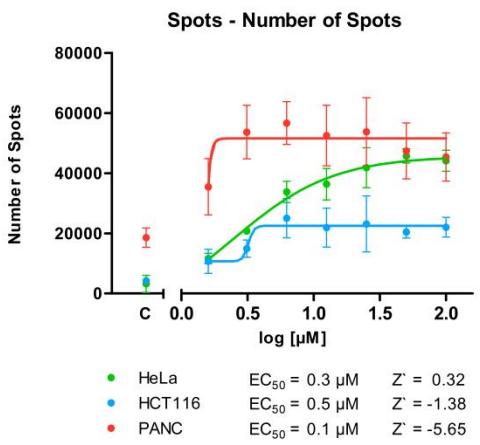
细胞自噬研究

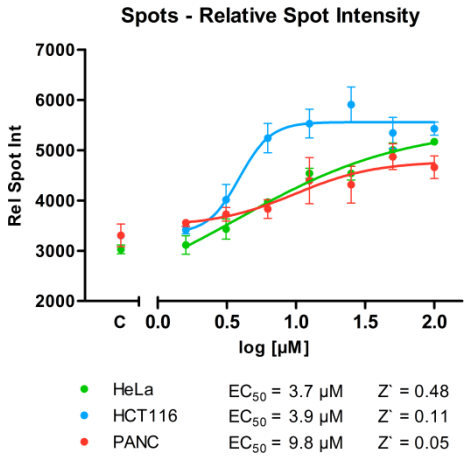
Data generated in the PerkinElmer Application Lab, Hamburg

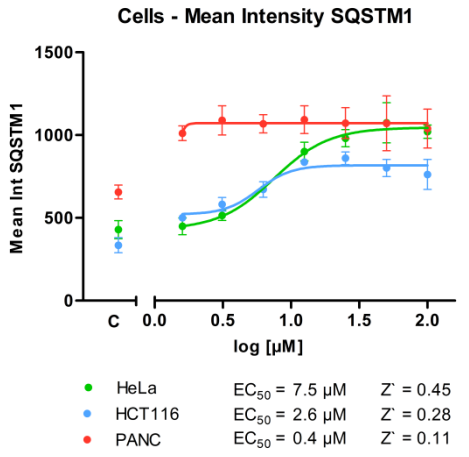
Autophagy in three cell lines

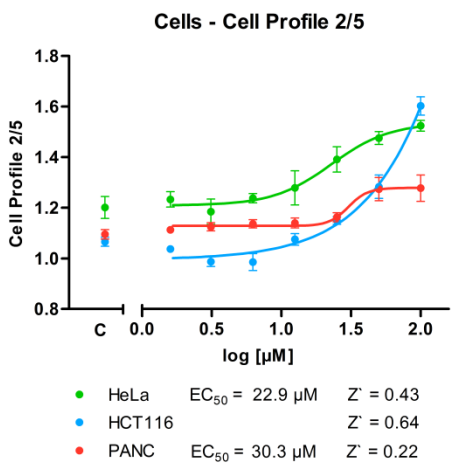


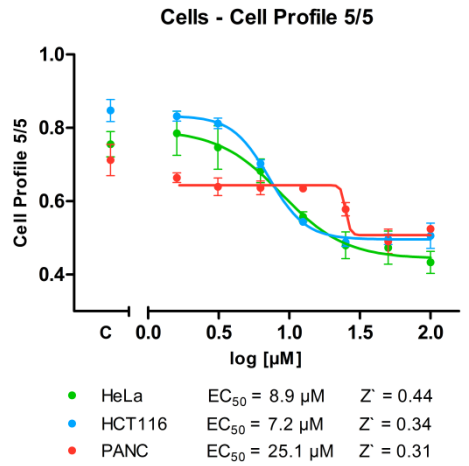
Examples of individual properties

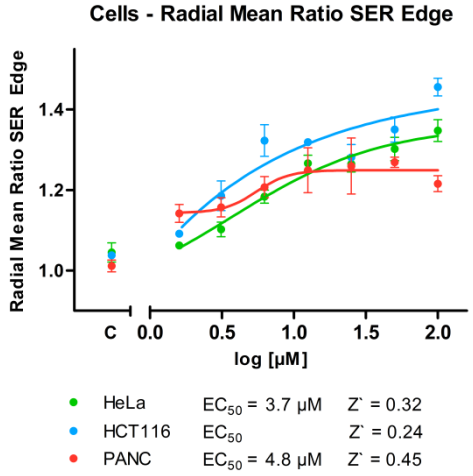












Phenotypic change not sufficiently described for all three cell lines

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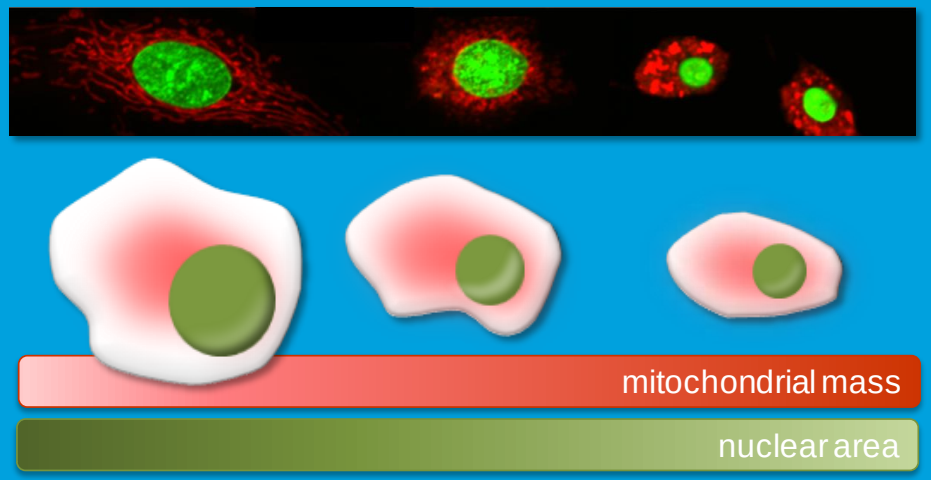
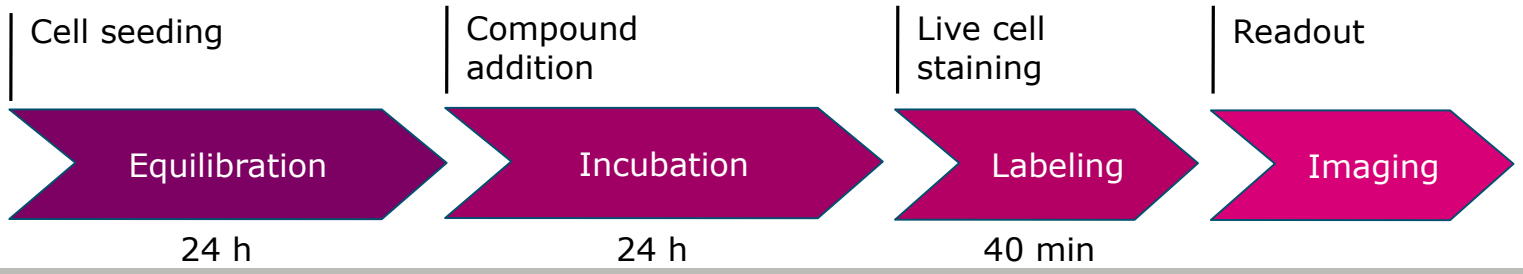
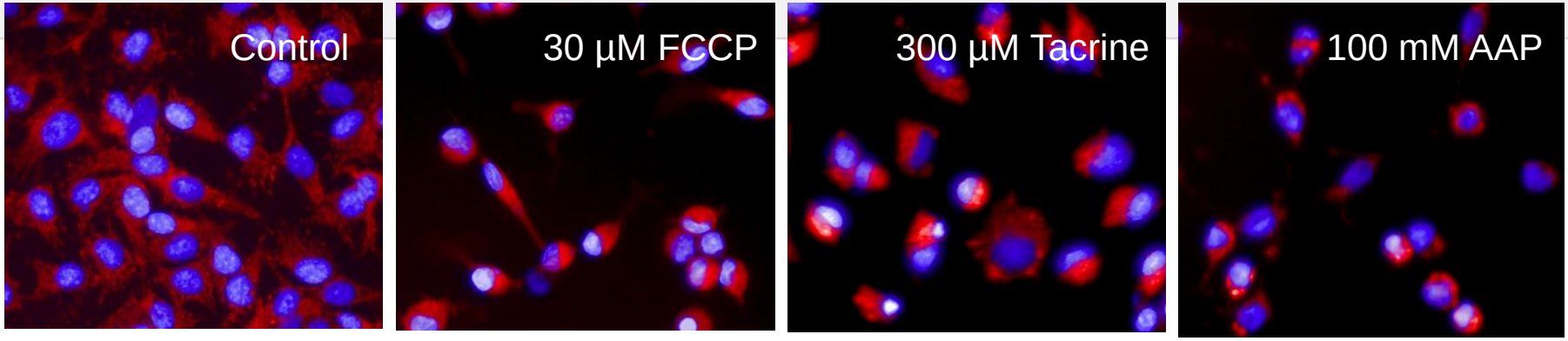


细胞毒性研究

Data generated in the PerkinElmer Application Lab



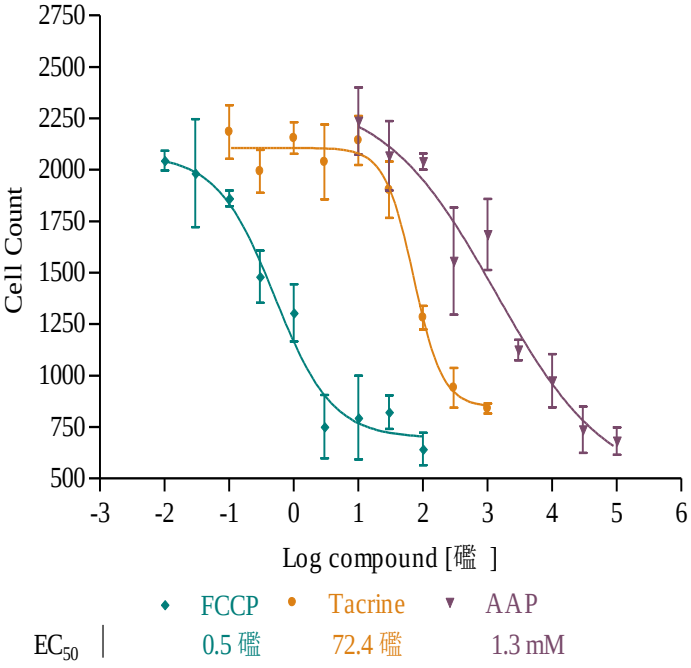
细胞毒性

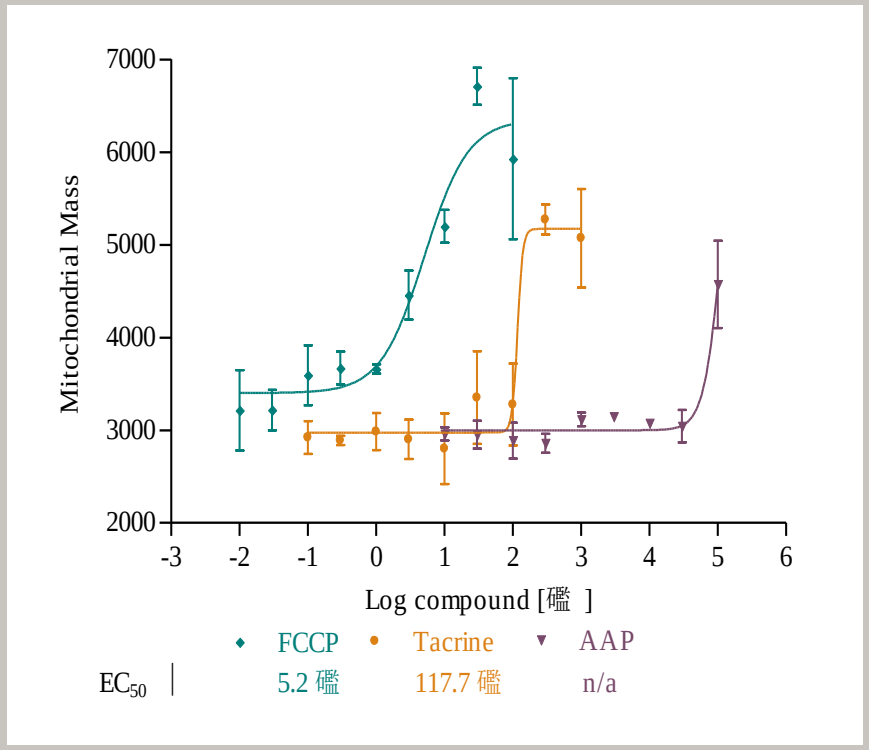


细胞计数	Hoechst 33342
线粒体数量	MitoTracker® Deep Red
细胞核增大/皱缩	Hoechst 33342

- 20x long WD 物镜成像
- 对HepG2细胞进行3种化合物处理（Carbonyl Cyanide P-(Trifluoromethoxy) Phenylhydrazone , Tacrine and Acetaminophen），观察到细胞毒性
- 处理后细胞数量减少，线粒体数量增多，细胞核变小

细胞毒性

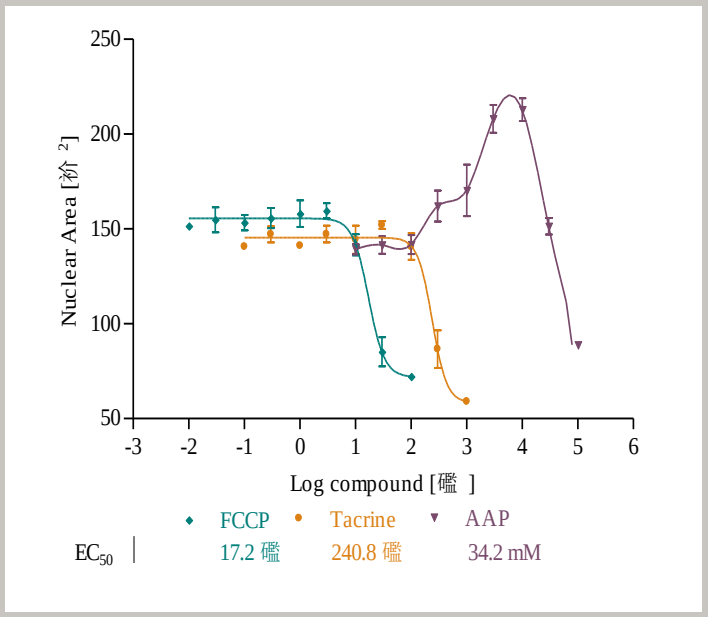


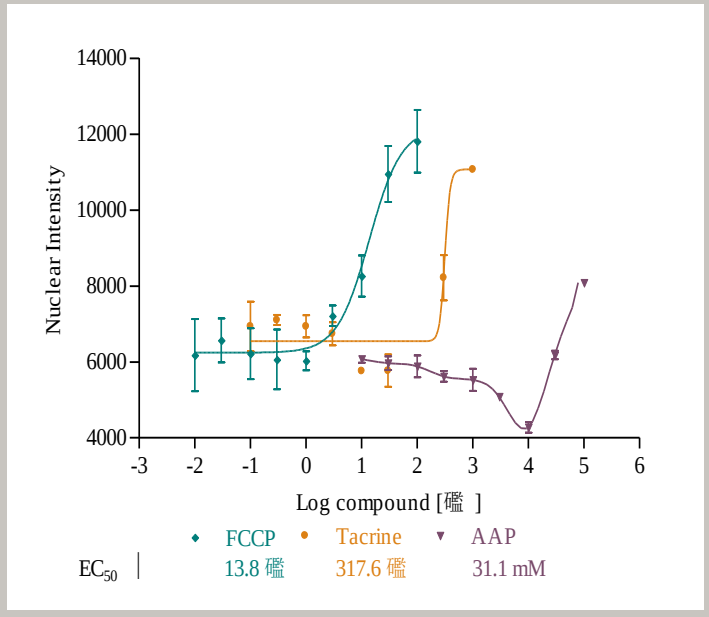


细胞数目变化与化合物浓度的关系，随药物浓度增加，细胞数目逐渐减少

线粒体密度的曲线:
线粒体在细胞毒作用早期就受到影响，这里线粒体功能紊乱主要表现为线粒体呼吸作用增强

细胞活性检测结果II- 细胞核面积和荧光强度





- 细胞损伤后通常会造成细胞核皱缩
- FCCP 和 Tacrine 导致细胞核皱缩，同时细胞核荧光强增大
- AAP 最初导致细胞核增大，很可能是因为诱导细胞坏死，然后细胞核皱缩
- 高内涵支持我们做多个浓度梯度，支持我们同时做多个维度的表型分析，有助于我们发现这些隐藏的但实际上很重要的表型，有助于对化合物作用机制进行分类。

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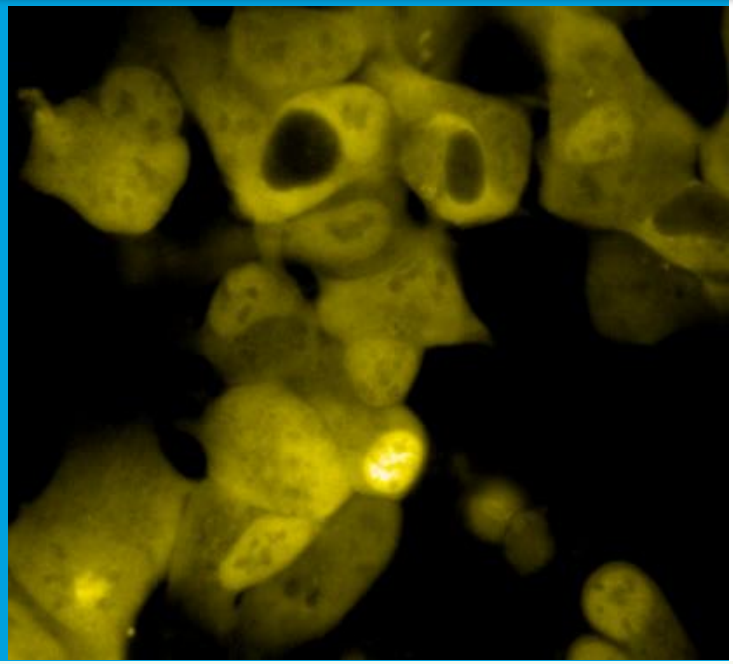


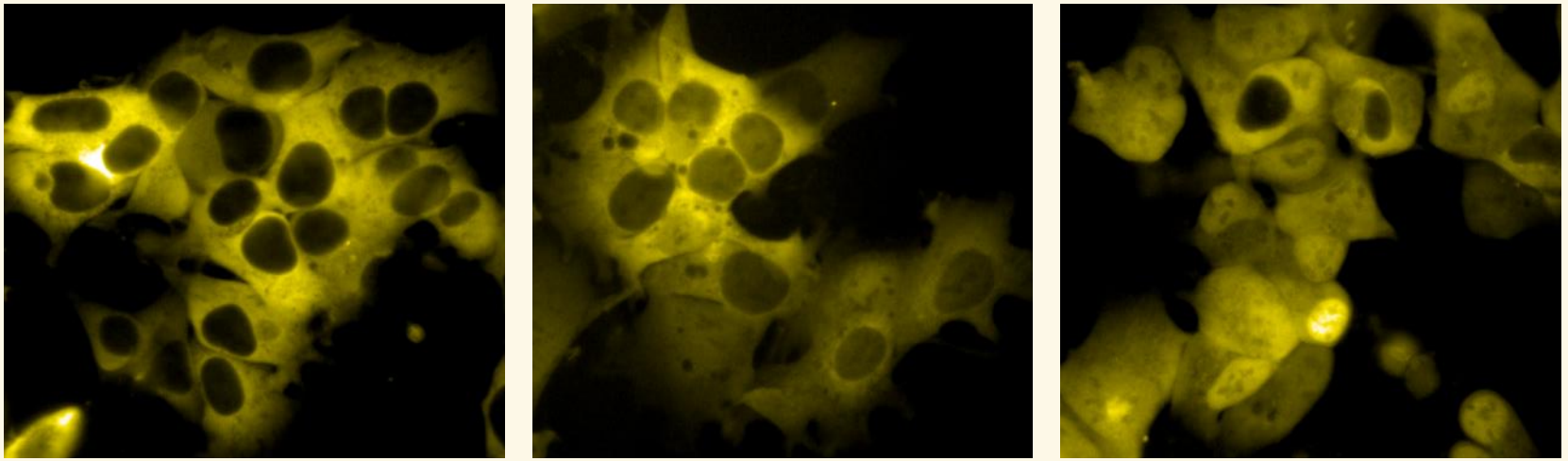
蛋白转位研究

Data generated in the PerkinElmer Application Lab

蛋白转位　在活细胞内分析NF-κB 动态变化

HaloTag® TMR ligand染活细胞

HaloTag® TMR ligand (fused to p65 subunit of NF-κB); 30 min post-TNFα addition



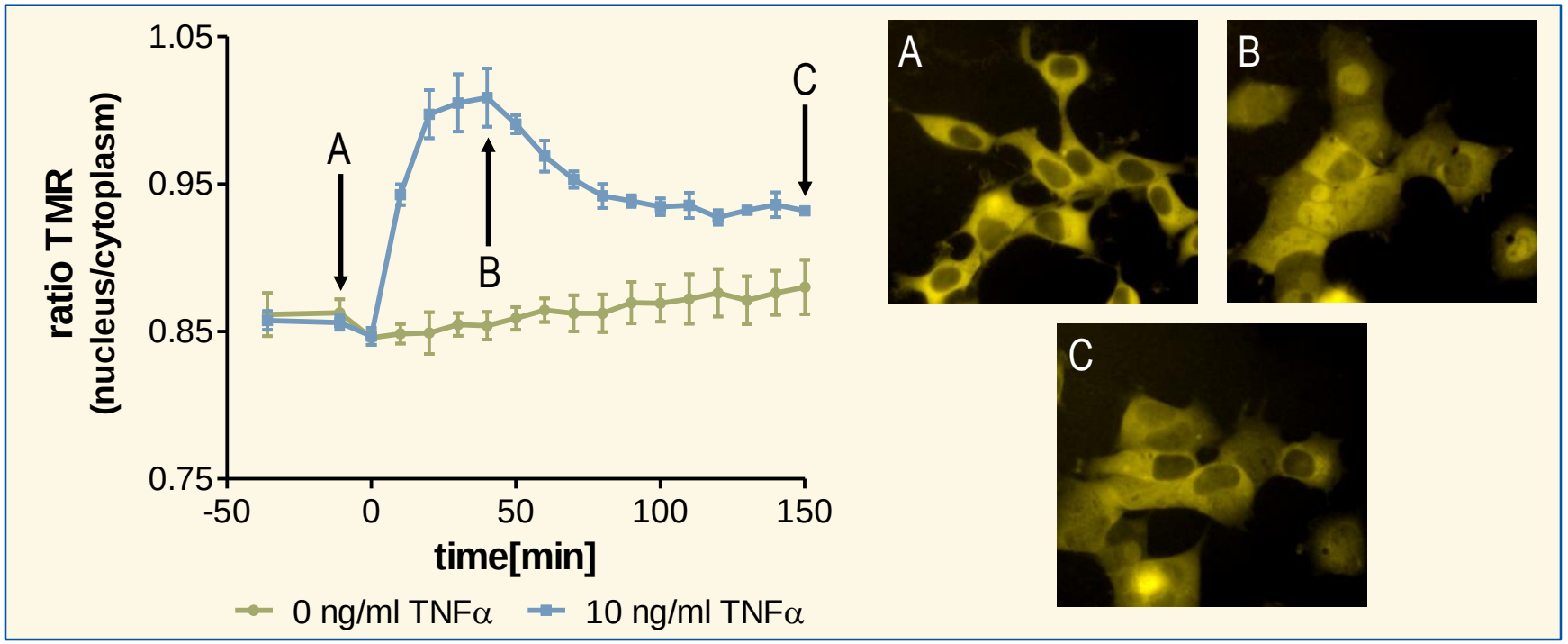
0 ng/ml TNFα　　0.5 ng/ml TNFα　　50 ng/ml TNFα

- HEK293细胞稳定表达NF-κB家族 带 HaloTag® 融合标签的p65 (p65-HT)，通过HaloTag® TMR 配体透过细胞膜染活细胞
- 用不同浓度TNFα 刺激NF-κB 信号
- 用Operetta® 高内涵系统成像，40x LWD 物镜荧光宽场

TNFα induces nuclear import of p65

NF-κB转位具有时间效应

- 通过Harmony® 高内涵成像和分析软件计算
- 计算NF-κB荧光 信号的核质比



- 刺激30min后，核内p65-HT百分比 达到最高值
- 与固定终点分析相反，向实验中添加时间维度，允许鉴定抑制NF-κB易位的化合物以及影响细胞核中NF-κB分子驻留时间的化合物

Live cell imaging allows the study of signaling dynamics

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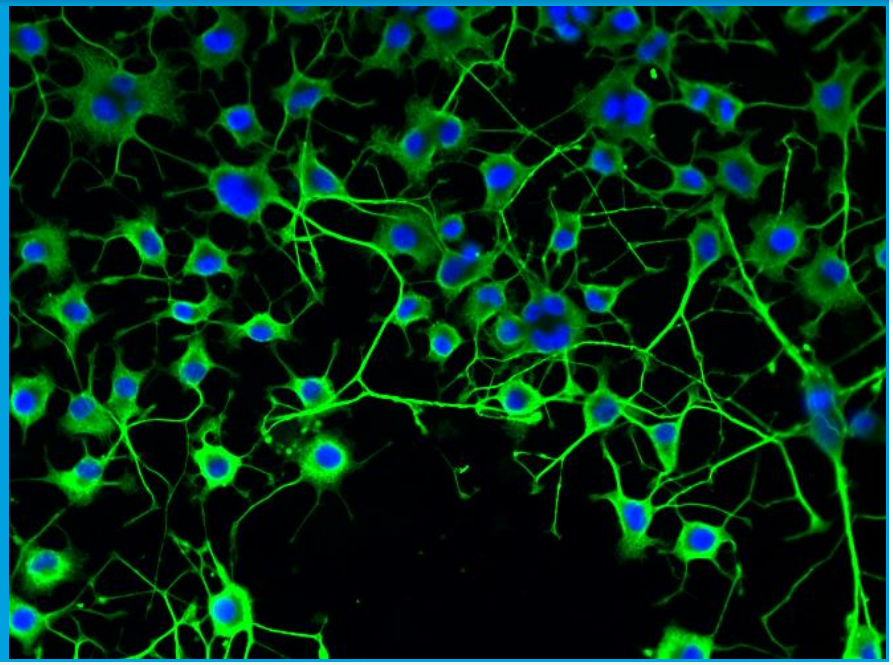
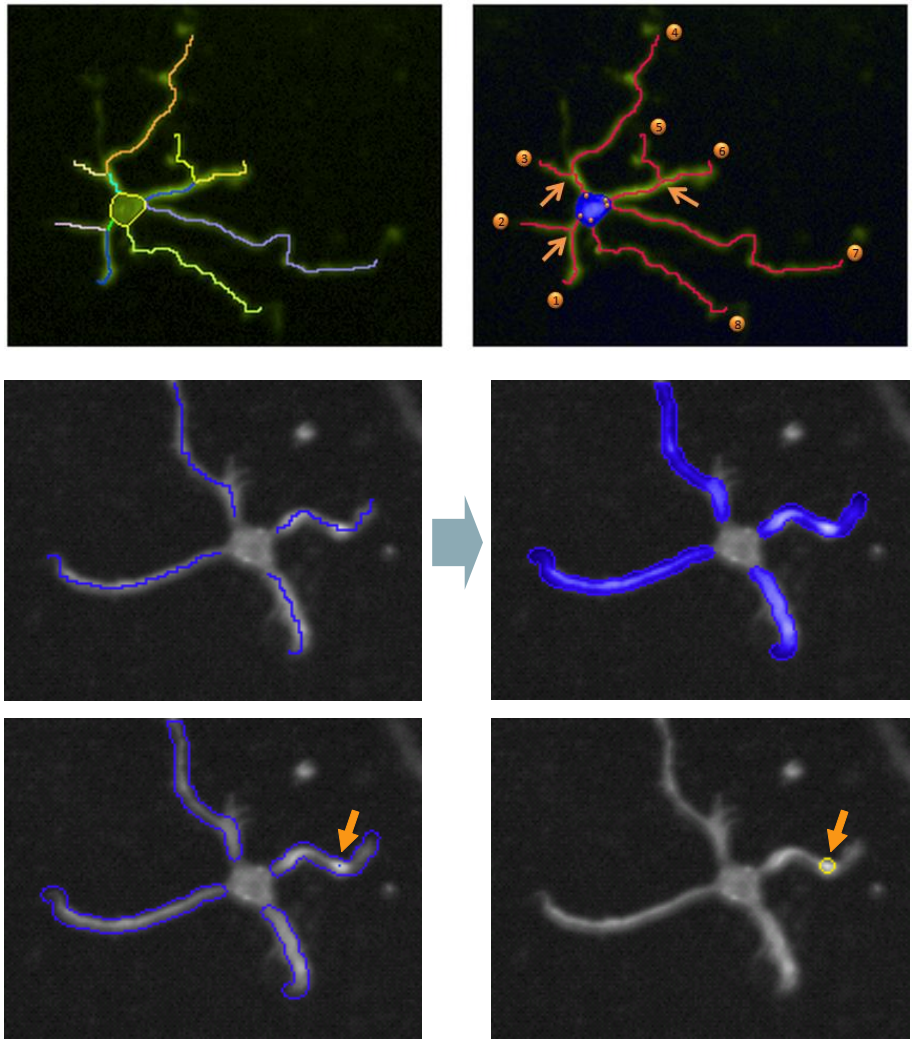


神经细胞研究

Data generated in the PerkinElmer Application Lab

独有的神经突触分析模块 – 相关分析

- Powerful neurite analysis
  - Left: individual segments (different colors)
  - Right: Roots (circles), nodes (arrows), and ends (numbers)
- Unique colocalization analysis
  - Neurites can be used as search mask for signals colocalized on neurites ⇨ essential for axon analysis
  - Middle: mask created from neurites
  - Lower: Spot identification on neurite (arrow)

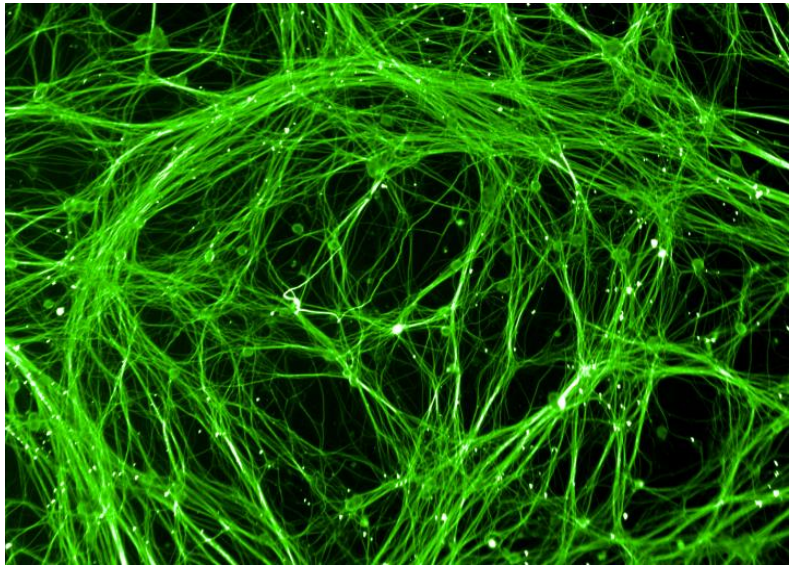


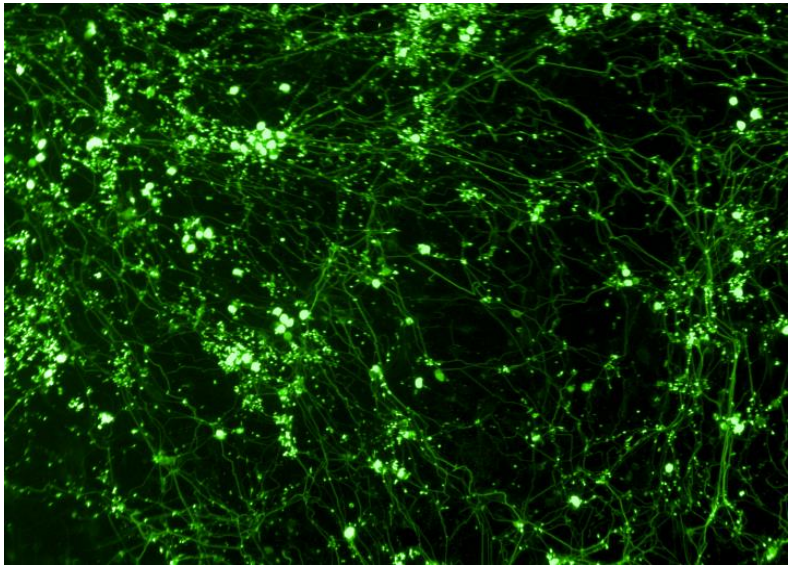
神经损伤表型研究

NGF treated

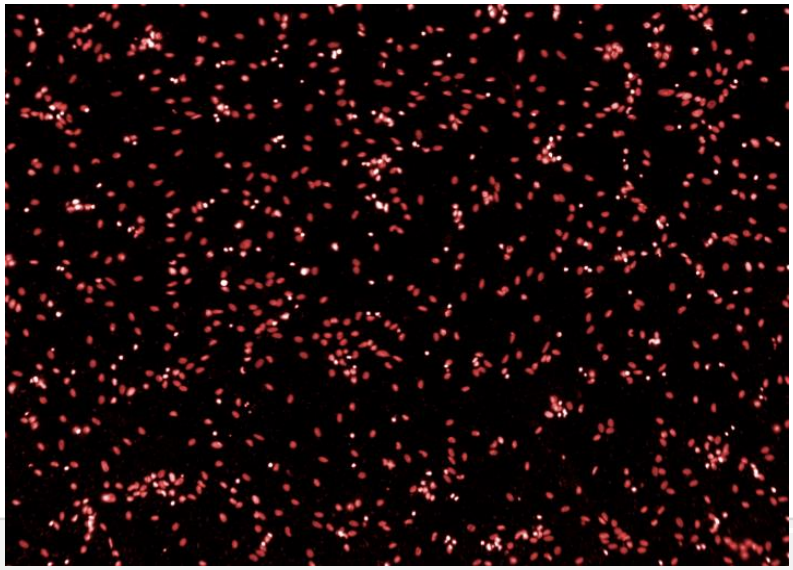
infected

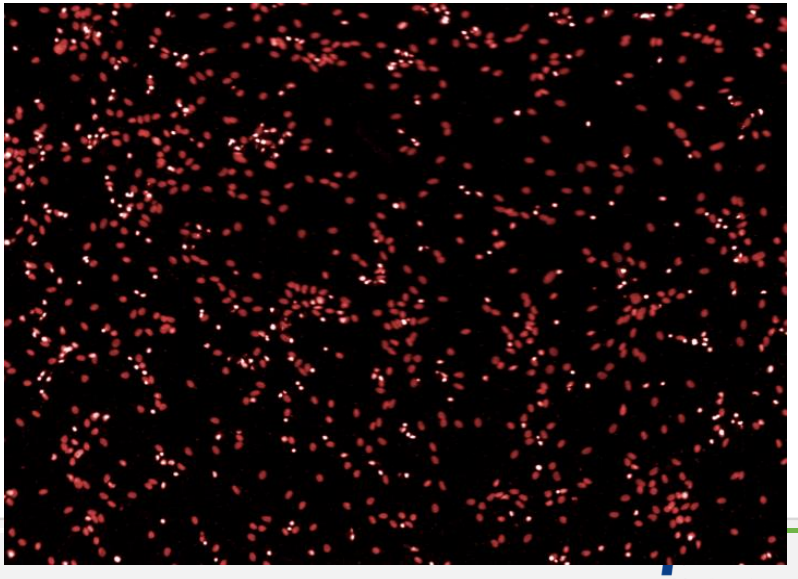
Tuj1-A488
Axons





Draq5
Nuclei





友泽仁信 Youze renxin

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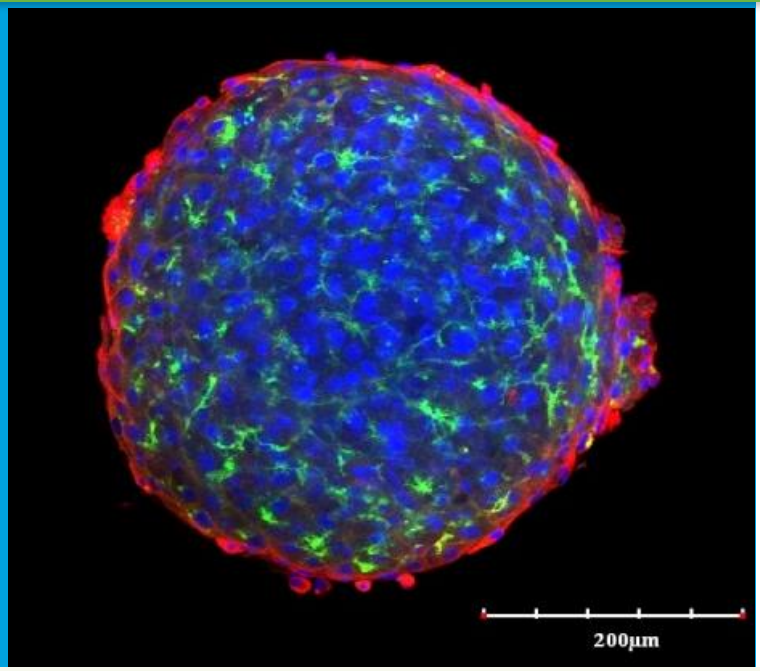


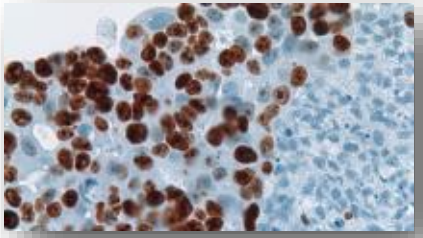
3D微组织研究

Data generated in the PerkinElmer Application Lab

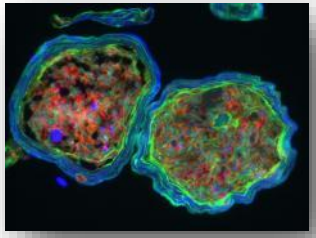
Immunofluorescence image of hepatocytes co-cultured with non parenchymal cells (NPC).
Green: DPP-IV (bile canalicular marker),
Blue: DAPI,
Red: ICAM-1 (endothelial marker)

What are Microtissues (MTs) or Spheroids?

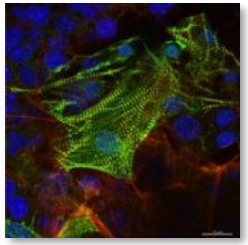
- 自组装的细胞群
- 体外三维细胞模型：最接近体内的模型 《Nature medicine》
- 细胞产生内源性细胞外基质（ECM）
- 细胞 - 细胞和细胞 - ECM相互作用
- 不同的细胞可以长成MT ...



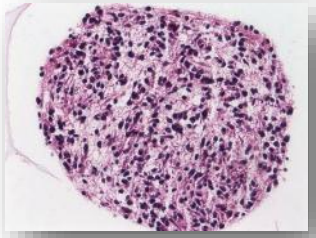
Tumor MTs



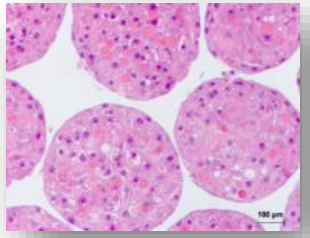
Skin MTs



Embryoid Bodies



Neuro MTs



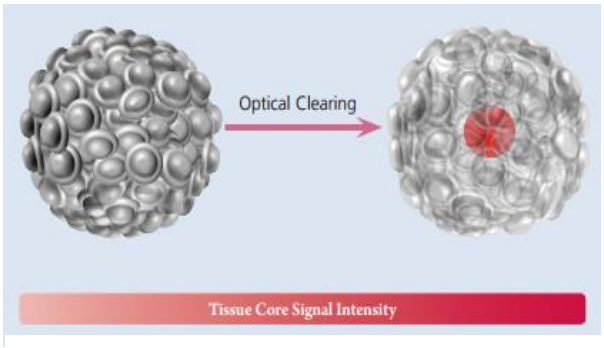
Liver MTs

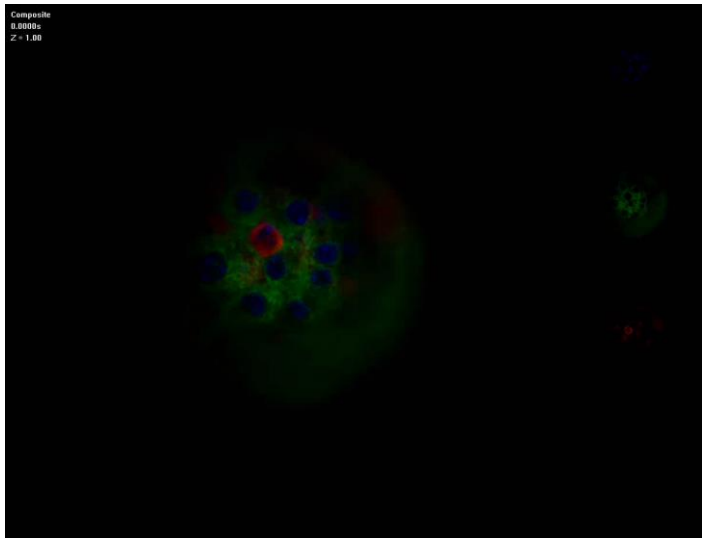
Physiologically relevant 3D cell model

Data courtesy of InSphero

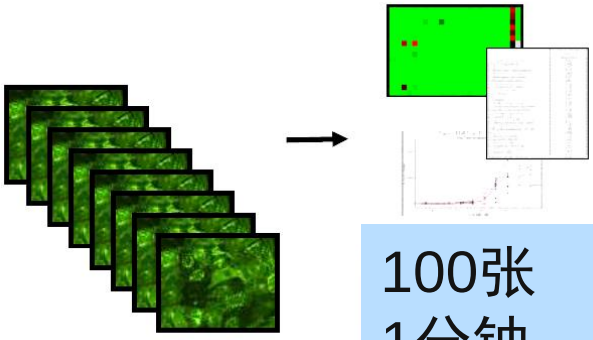
HCS benefit

水镜—
Z轴更深扫描深度



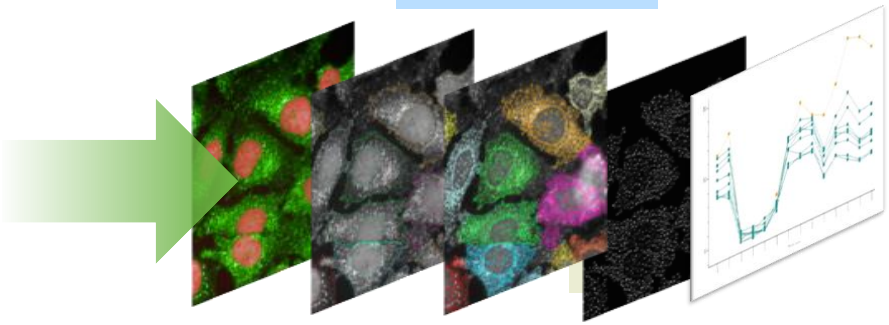


更快的扫描速度



100张
1分钟

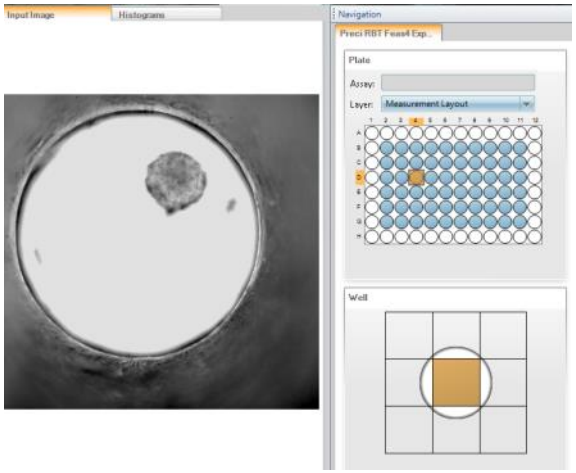
全面的分析功能

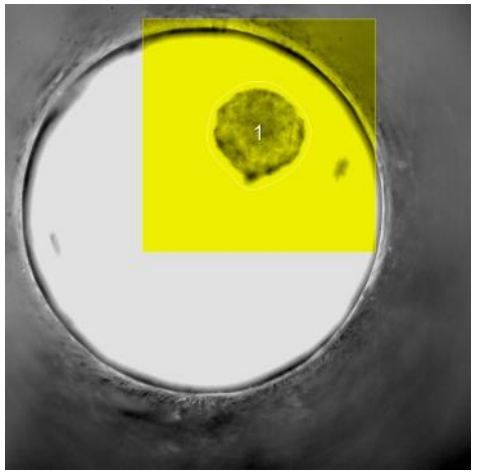


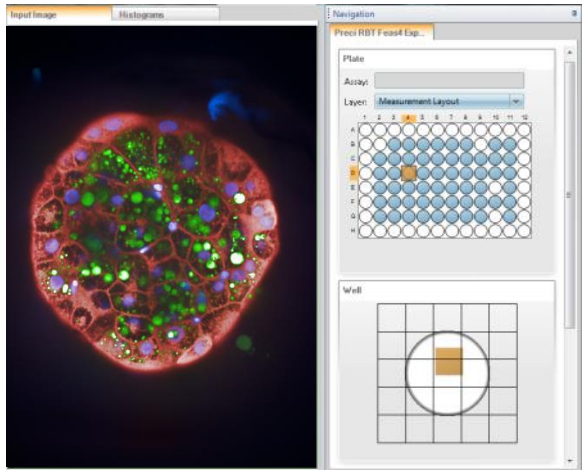
特色模块 Intelligent Acquisition – PreciScan

PreciScan

PreScan – Meas (10x) → „Find Microtissue“ Analysis → ReScan – Meas (40x)



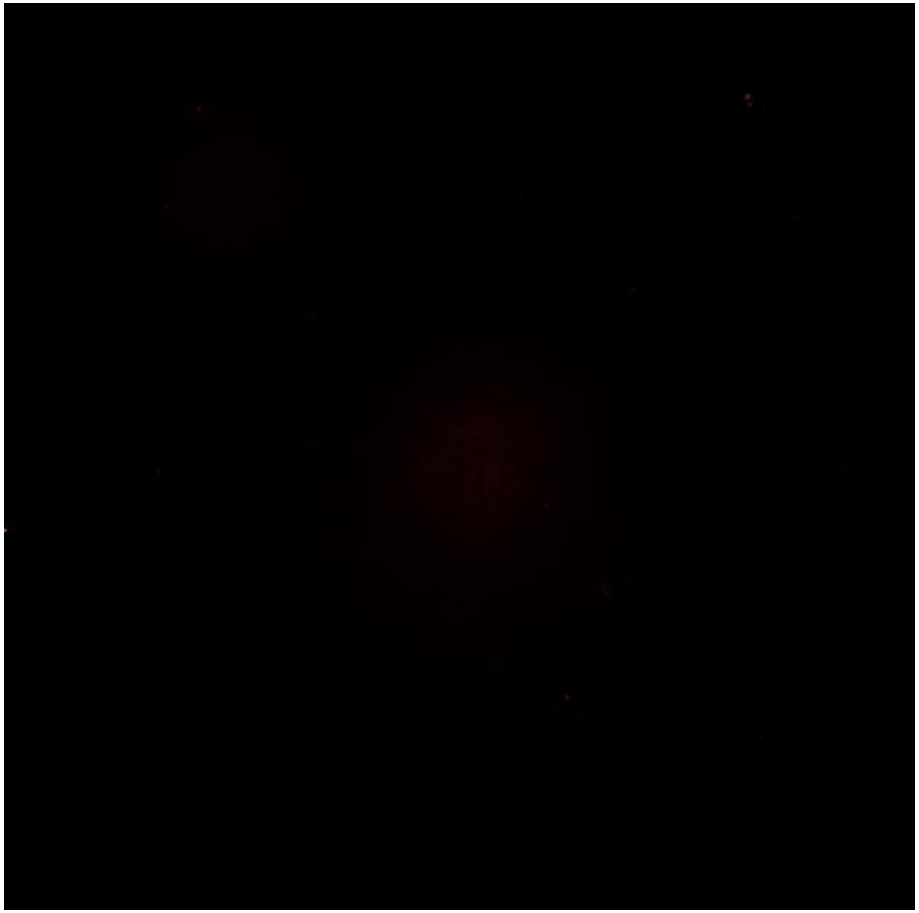


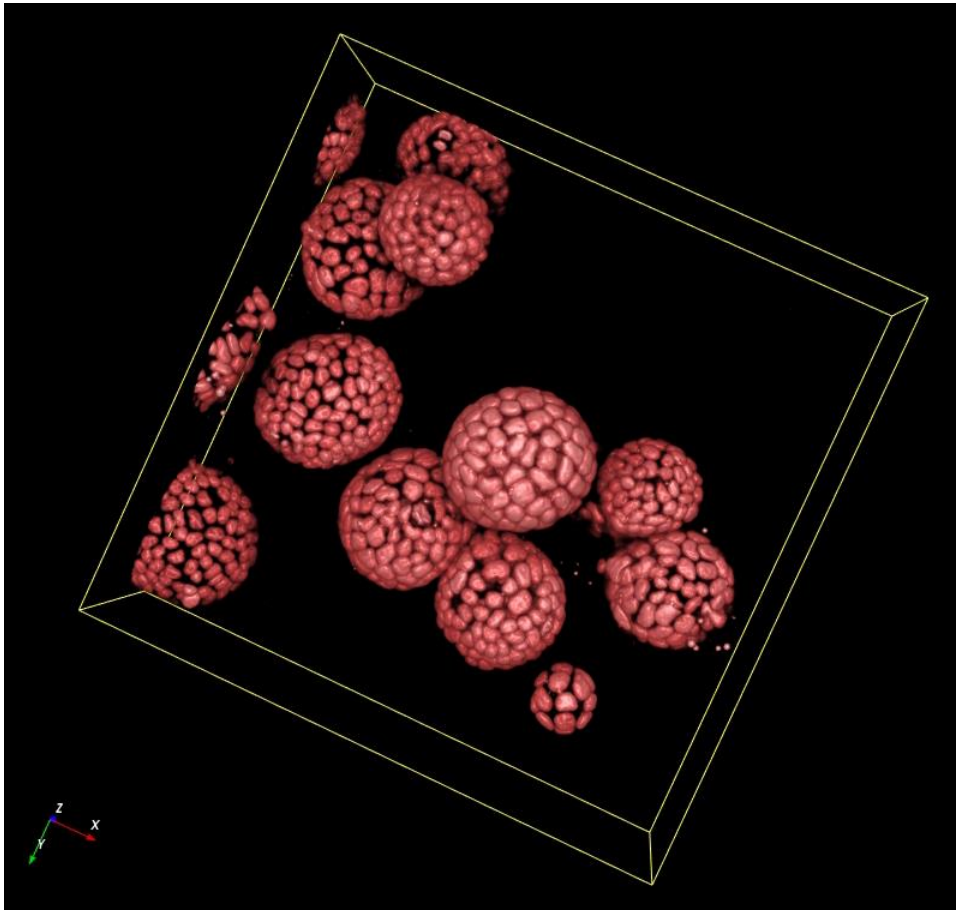


Identify x/y positions of tissues for ReScan measurement

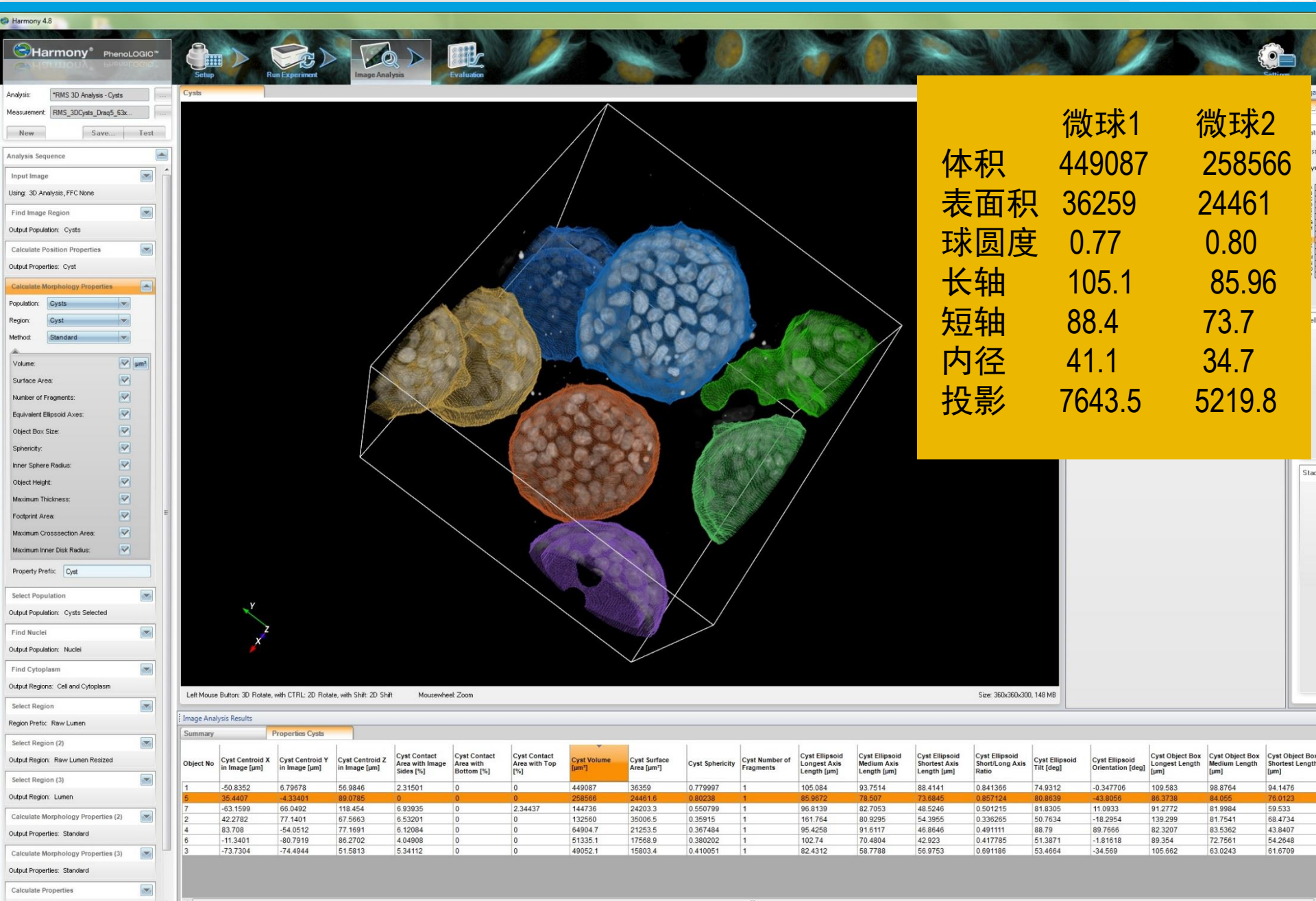
ReScan only wells that contain tissues

3D重构视图与分析





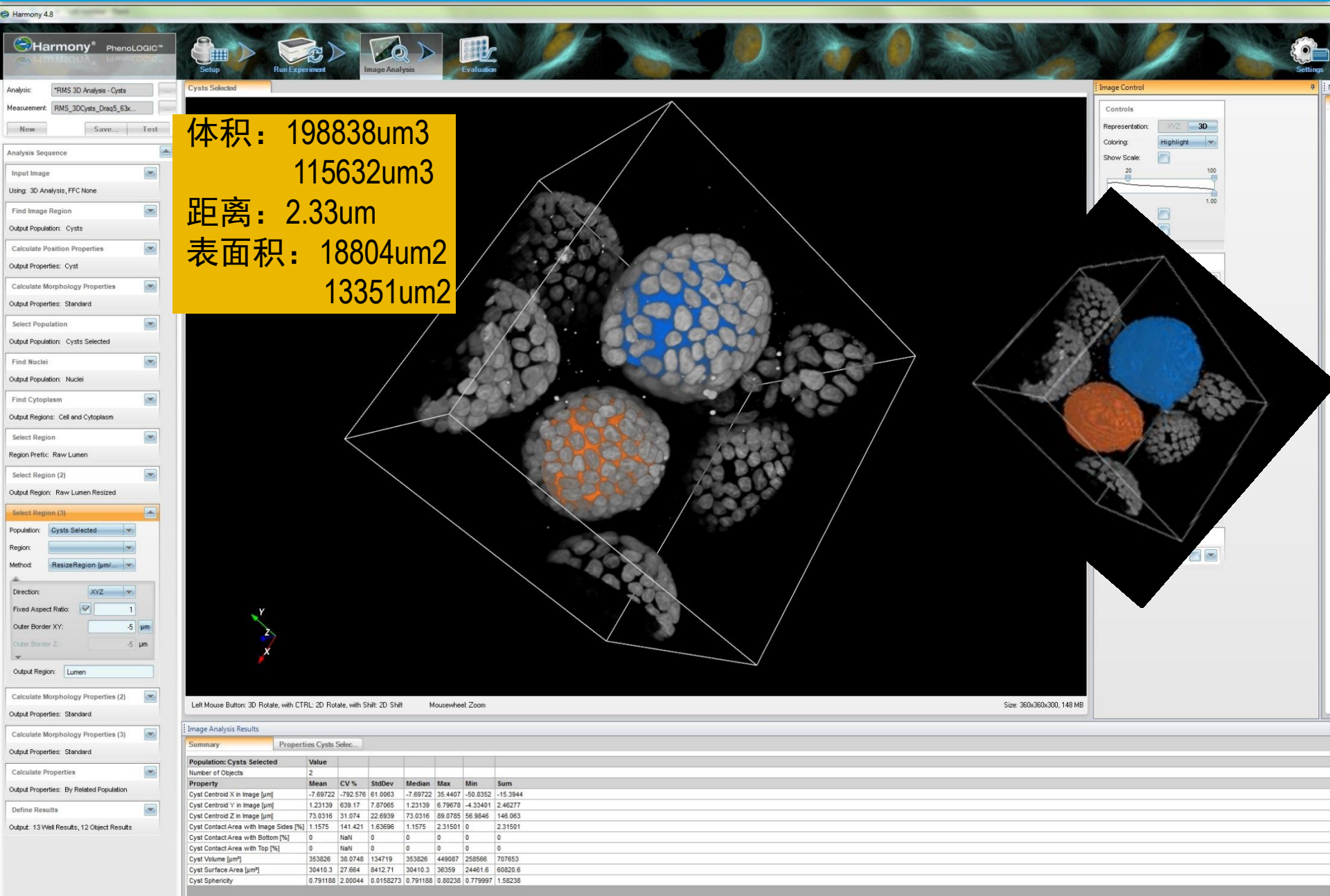
肾微组织体积等参数计算



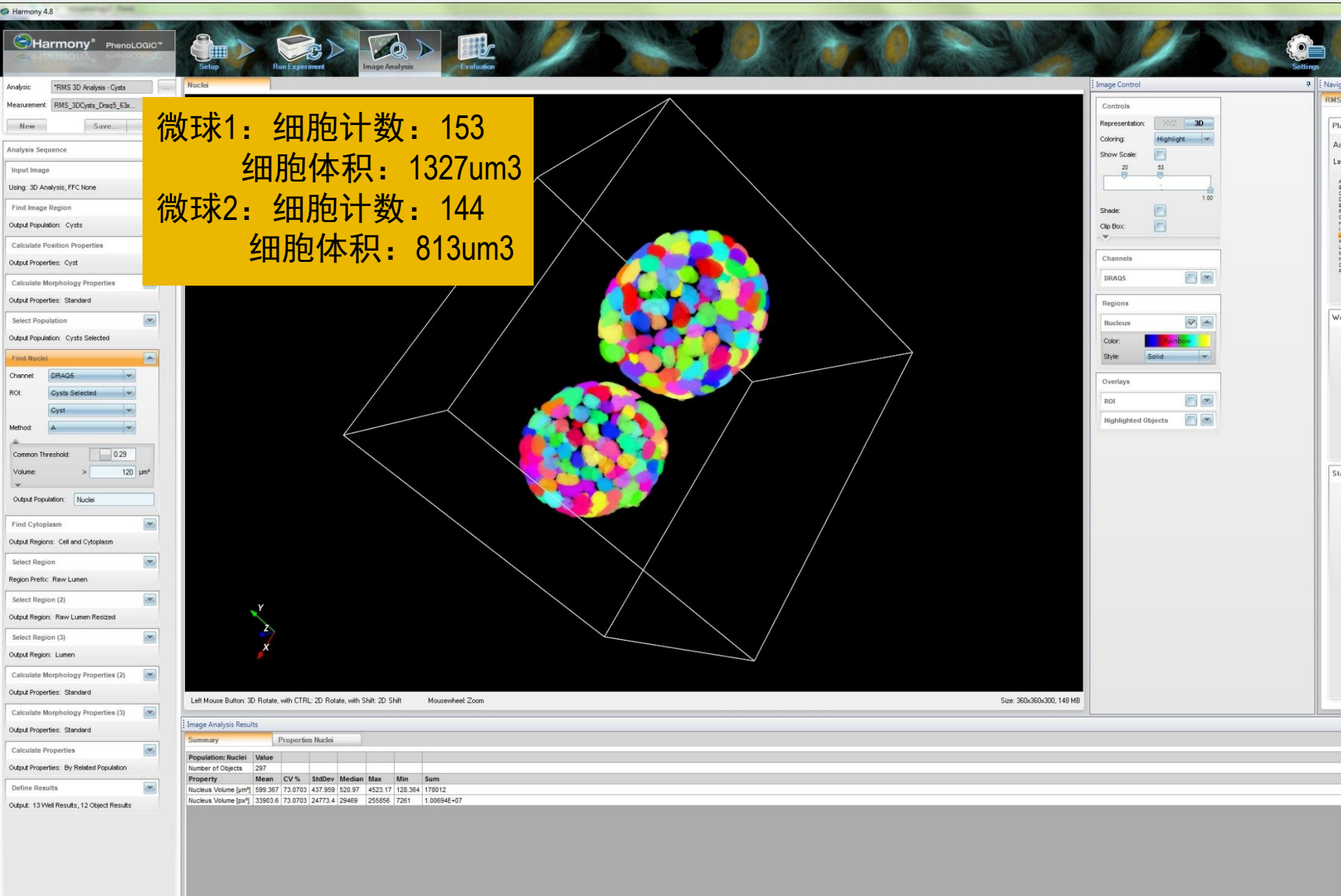
Object No	Cyst Centroid X in Image [µm]	Cyst Centroid Y in Image [µm]	Cyst Centroid Z in Image [µm]	Cyst Contact Area with Image Sides [%]	Cyst Contact Area with Bottom [%]	Cyst Contact Area with Top [%]	Cyst Volume [µm³]	Cyst Surface Area [µm²]	Cyst Sphericity	Cyst Number of Fragments	Cyst Ellipsoid Longest Axis Length [µm]	Cyst Ellipsoid Medium Axis Length [µm]	Cyst Ellipsoid Shortest Axis Length [µm]	Cyst Ellipsoid Short/Long Axis Ratio	Cyst Ellipsoid Tilt [deg]	Cyst Ellipsoid Orientation [deg]	Cyst Object Box Longest Length [µm]	Cyst Object Box Medium Length [µm]	Cyst Object Box Shortest Length [µm]
1	-50.8352	6.79678	56.9846	2.31501	0	0	449087	36359	0.779997	1	105.084	93.7514	88.4141	0.841366	74.9312	-0.347706	109.583	98.8764	94.1476
5	35.4407	-4.33401	89.0785	0	0	0	258566	24461.6	0.80238	1	85.9672	78.507	73.6845	0.857124	80.8639	-43.8056	86.3738	84.055	76.0123
7	-63.1599	66.0492	118.454	6.93935	0	2.34437	144736	24203.3	0.550799	1	96.8139	82.7053	48.5246	0.501215	81.8305	11.0933	91.2772	81.9984	59.533
2	42.2782	77.1401	67.5663	6.53201	0	0	132560	35006.5	0.35915	1	161.764	80.9295	54.3955	0.336265	50.7634	-18.2954	139.299	81.7541	68.4734
4	83.708	-54.0512	77.1691	6.12084	0	0	64904.7	21253.5	0.367484	1	95.4258	91.6117	46.8646	0.491111	88.79	89.7666	82.3207	83.5362	43.8407
6	-11.3401	-80.7919	86.2702	4.04908	0	0	51335.1	17568.9	0.380202	1	102.74	70.4804	42.923	0.417785	51.3871	-1.81618	89.354	72.7561	54.2648
3	-73.7304	-74.4944	51.5813	5.34112	0	0	49052.1	15803.4	0.410051	1	82.4312	58.7788	56.9753	0.691186	53.4664	-34.569	105.662	63.0243	61.6709

	微球1	微球2
体积	449087	258566
表面积	36259	24461
球圆度	0.77	0.80
长轴	105.1	85.96
短轴	88.4	73.7
内径	41.1	34.7
投影	7643.5	5219.8

腔内体积



微球内细胞计数



Harmony 4.8

Harmony® PhenoLOGIC™

Setup | Run Experiment | Image Analysis | Evaluation | Settings

Analysis: *3D distance tx untouched cell

Measurement: G1 – Measurement 1b

Load PreScan | New | Save... | Test

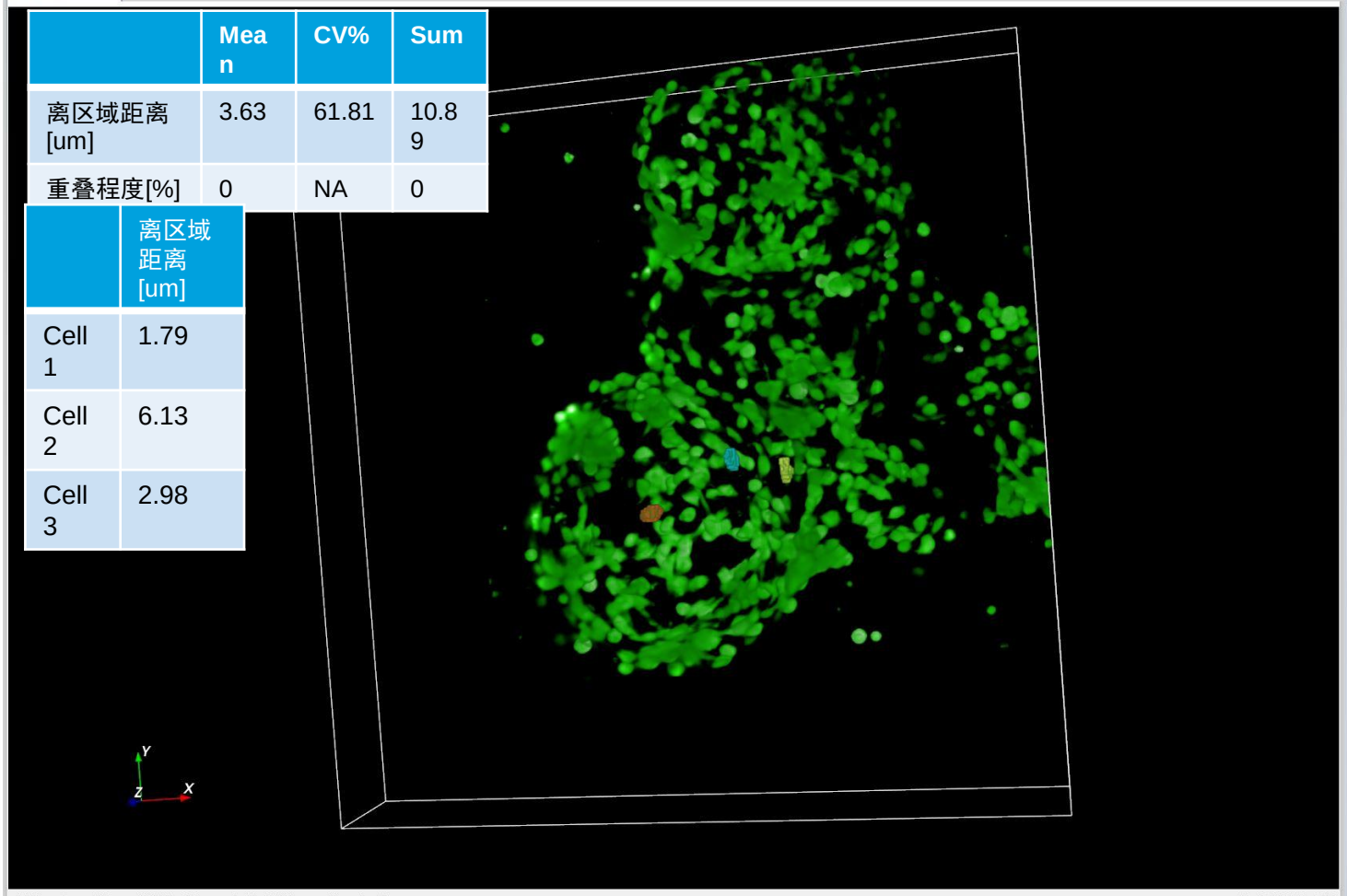
Analysis Sequence

- Input Image — Using: 3D Analysis, FFC None
- Find Image Region — Output Population: Image Region
- Select Region — Output Region: Image Region Resized
- Find Image Region (2) — Output Population: Image Region (2)
- Calculate Morphology Properties — Output Properties: Standard
- Calculate Position Properties — Output Properties: Image Region
- Select Population — Output Population: Image Region (2) Selected
- Select Population (2) — Output Population: Image Region (2) Selected S...
- Select Population (3) — Output Population: cell selected
- Calculate Position Properties (2)
  - Population: cell selected
  - Region: Image Region
  - Method: Cross Population
  - Population B: Image Region
  - Region B: Image Region
  - ROI Border Distance:
  - Nearest Object Distance:
  - Overlap:
  - Property Prefix: Image Region
- Define Results

cell selected

	Mean	CV%	Sum
离区域距离 [um]	3.63	61.81	10.89
重叠程度[%]	0	NA	0

	离区域距离 [um]
Cell 1	1.79
Cell 2	6.13
Cell 3	2.98



Left Mouse Button: 3D Rotate, with CTRL: 2D Rotate, with Shift: 2D Shift Mousewheel: Zoom Size: 360x360x35, 17 MB

Image Control

Controls — Representation: XYZ 3D; Coloring: Highlight; Show Scale; 27 80 0.61; Shade; Clip Box:

Channels

- Alexa 488 — Color: #1FF906; 217 8728 1.01; Auto Contrast:
- EthD-1 — Color: #20F807; 149 1341 0.83; Auto Contrast:

Regions — Image Region — Color: Rainbow; Style: Border

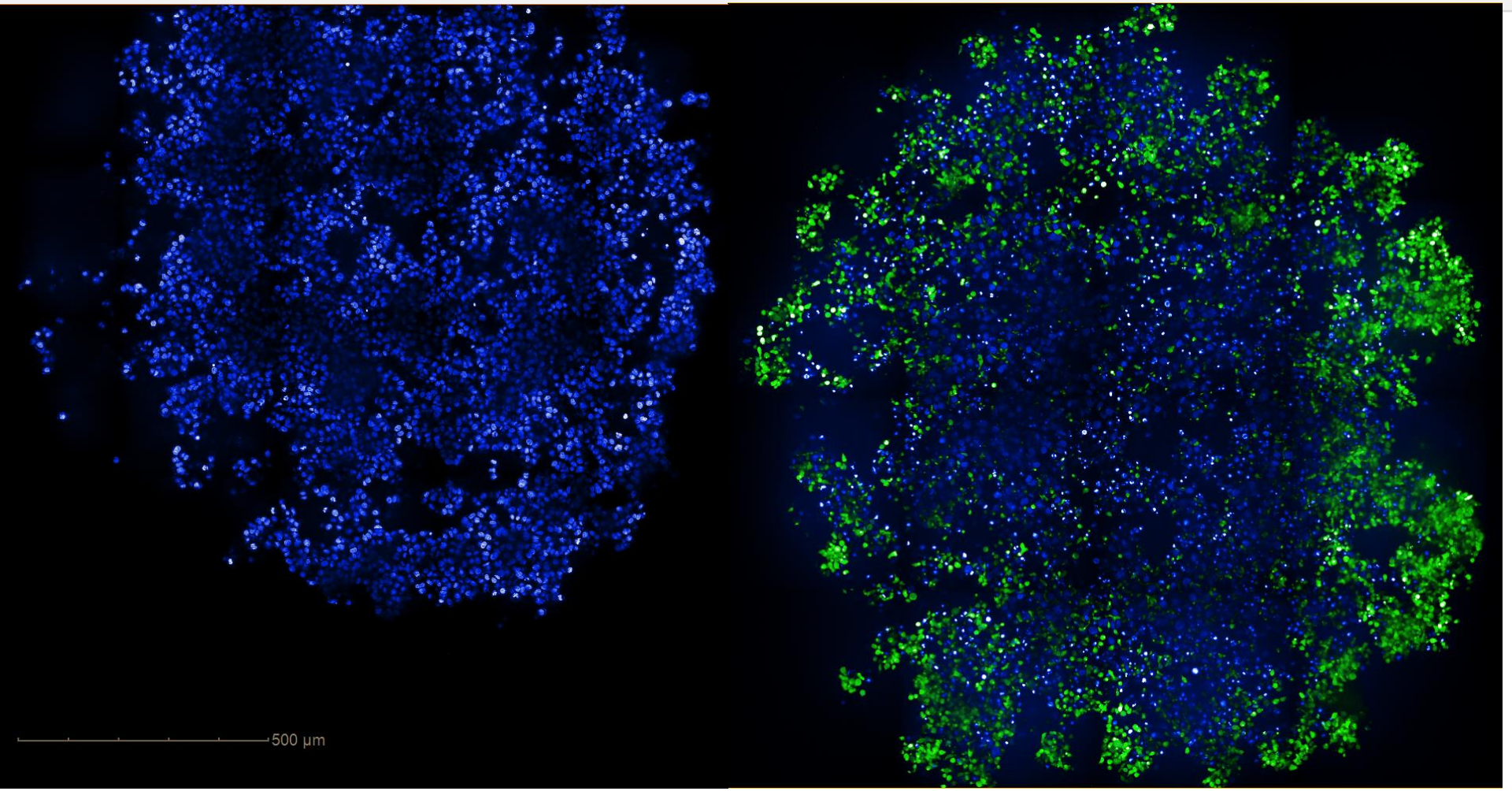
Overlays — Region B; Highlighted Objects

Image Analysis Results

Summary | Properties cell selected

Population: cell selected	Value						
Number of Objects	3						
Property	**Mean**	**CV %**	**StdDev**	**Median**	**Max**	**Min**	**Sum**
Image Region Volume [µm³]	2143.4	40.9582	877.898	1764.9	3147.06	1518.24	6430.21
Image Region Surface Area [µm²]	1073.02	23.8439	255.849	947.451	1367.39	904.213	3219.06
Image Region Centroid X in Well [µm]	-2091.77	-3.15185	65.9296	-2081.97	-2031.29	-2162.05	-6275.32
Image Region Centroid Y in Well [µm]	-384.594	-6.01409	23.1298	-376.559	-366.553	-410.67	-1153.78
Image Region Centroid Z in Well [µm]	52.6945	42.5511	22.4221	50.9614	75.9328	31.1892	158.083
Image Region Centroid X in Image [µm]	43.4212	151.837	65.9296	53.2211	103.902	-26.8598	130.264

3D微组织CAR-T杀伤实验

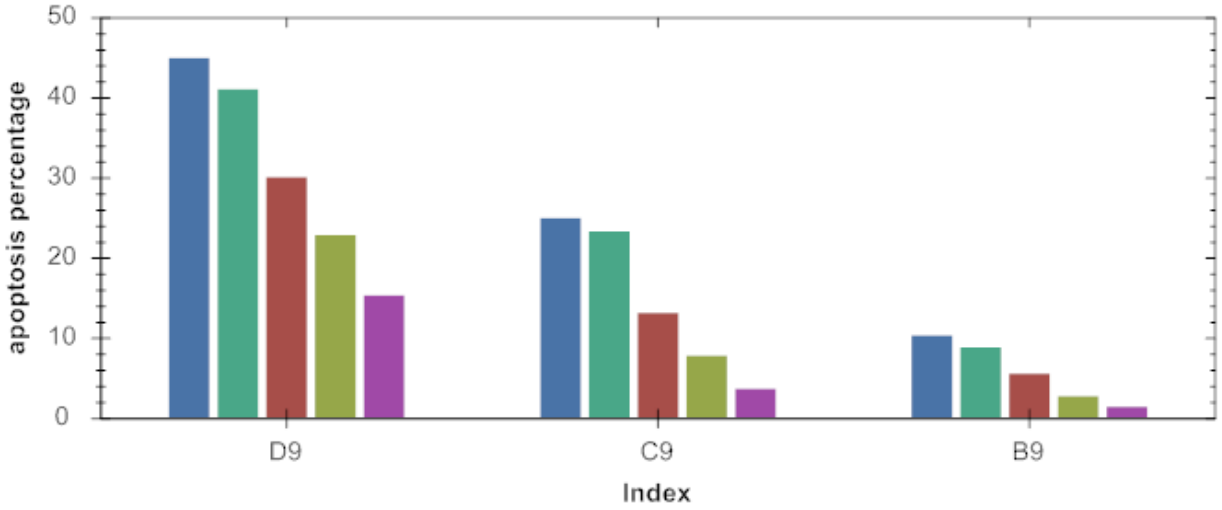


凋亡细胞检测　分层计算Car-T细胞浸润

PerkinElmer

分析结果

肿瘤凋亡细胞百分比

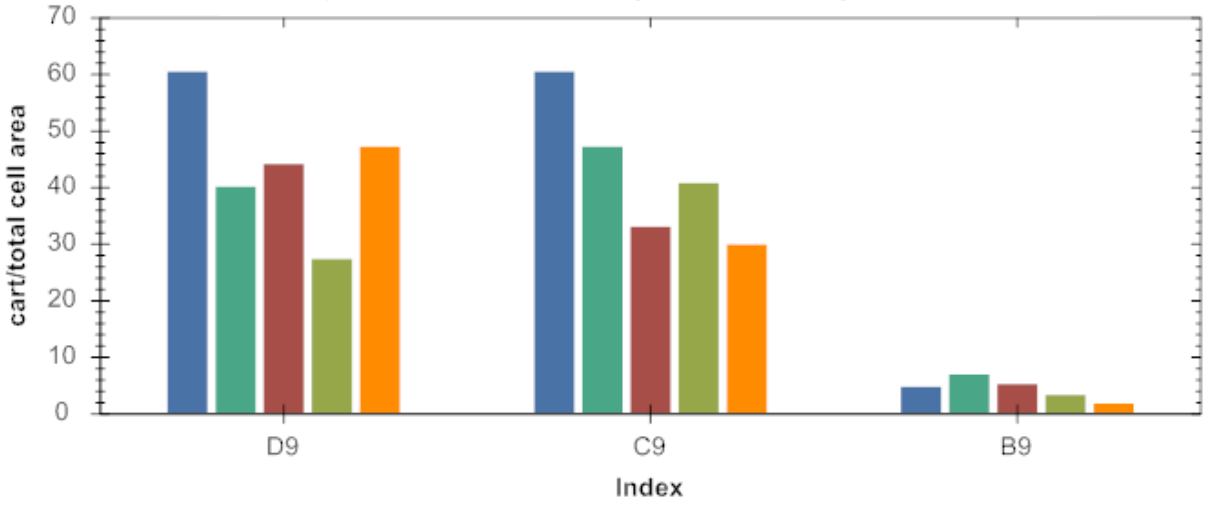


B9：癌细胞

C9：癌细胞+CAR-T a

D9：癌细胞+CAR-T b

每层CAR-T细胞面积/肿瘤面积* 100%



结论：

CAR-T a和b组会导致肿瘤凋亡

CAR-T 细胞侵润肿瘤与肿瘤凋亡有高度相关性

PerkinElmer

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… a representative cross-section

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东方肝胆医院	王红阳院士	罗氏中国研发中心	
重庆第三军医大学	万瑛	复旦大学 医学院	闻玉梅院士
中国中医科学院		中南大学湘雅医院 3台	
中国科学院上海生化细胞所 2台		首都医科大学	
厦门大学 分子疫苗学和分子诊断学国家重点实验室、药学院 2台		南京高新生物医药公共服务平台有限公司 2台	
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Harvard University

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ALTANA

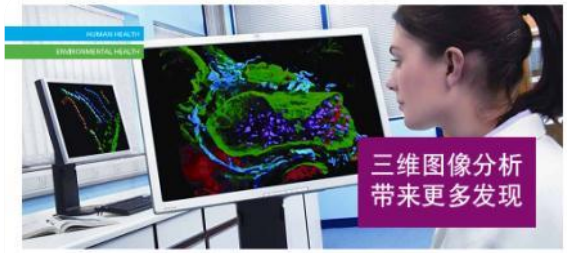
AstraZeneca INTERNATIONAL

AMGEN

Bristol-Myers Squibb

Pfizer

专业的高内涵技术交流活动。



Volocity三维细胞图像分析软件培训会——北京/上海

User Meetings

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整体解决方案——专业的应用支持团队

专业的应用支持团队

于雪梅

18340092170

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