xCELLigence system

Real time, label free, cells analysis

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Agenda

- **Technology concept and advantages**
- **Applications**
- **RTCA software**
- **Key features**

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- **Technology concept and advantages**
- Applications
- RTCA software
- Key features

The xCELLigence RTCA system

The xCELLigence System monitors **cellular events**

- **in real time**
- **without the incorporation of labels**
- **measuring electrical impedance across microelectrodes**

Impedance Biosensor Technology

Nature. 1993 Dec 9;366(6455):591-2.

A morphological biosensor for mammalian cells.

Giaever I, Keese CR.

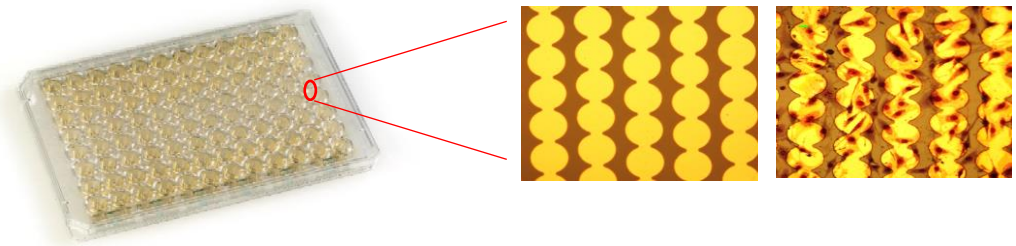
Source

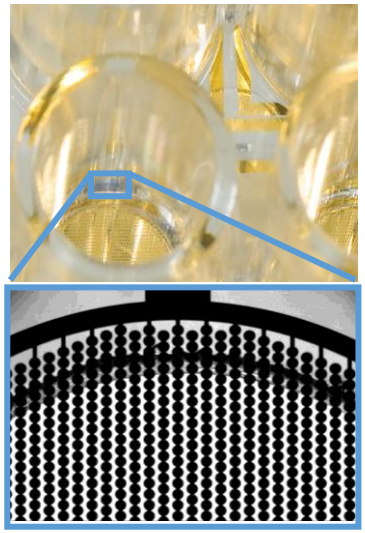
School of Science, Rensselaer Polytechnic Institute, Troy, New York 12180-3590.

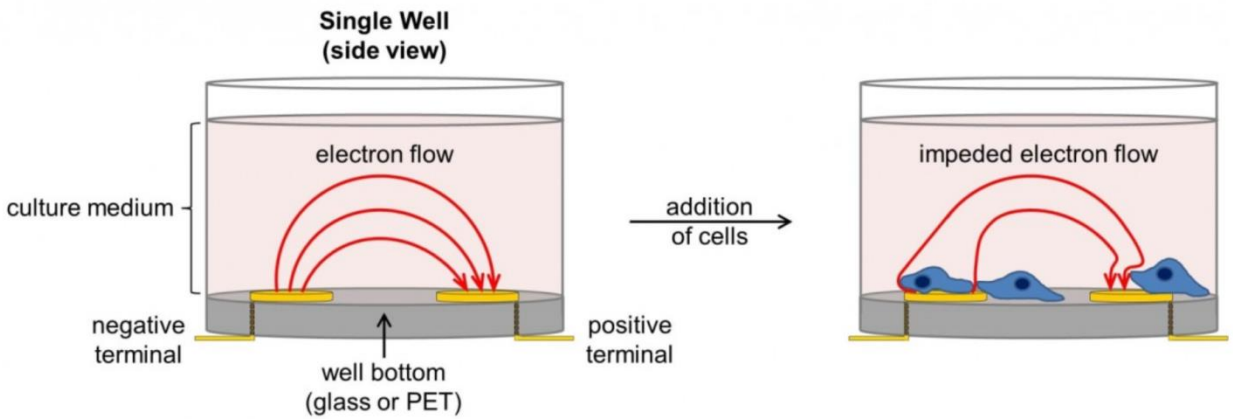
Abstract

An electrical biosensor is described that can continuously track morphological changes of adherent cells providing quantitative data from both sparse and confluent cultures. The method is capable of detecting vertical motion of cells of the order of 1 nm, much below the resolution of an optical microscope.

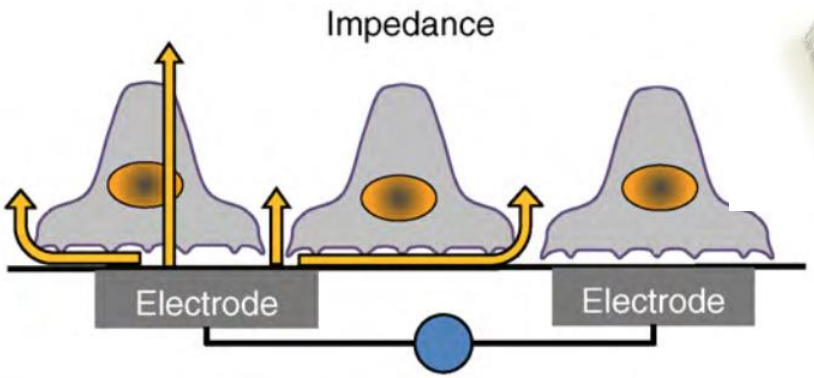
Concept: Impedance read-out

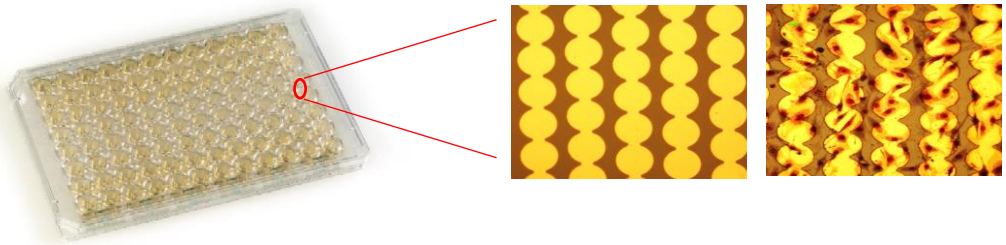




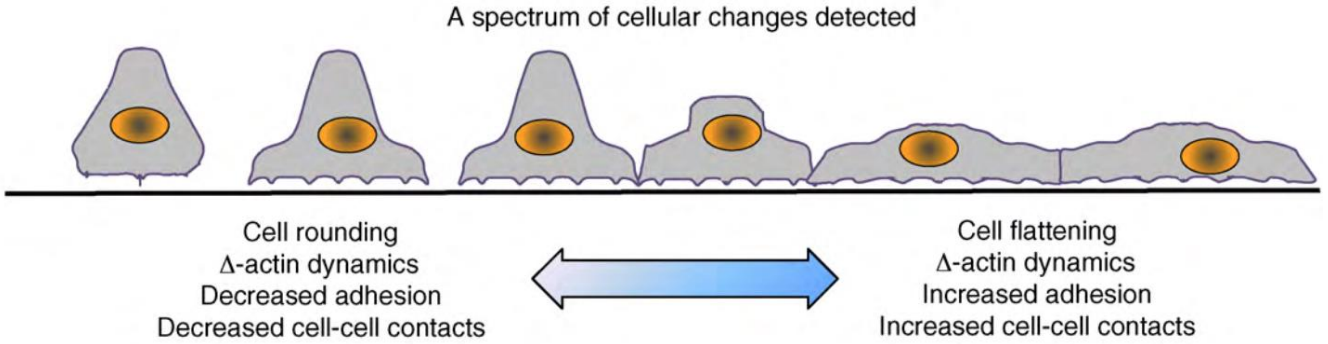


Concept: Impedance read-out



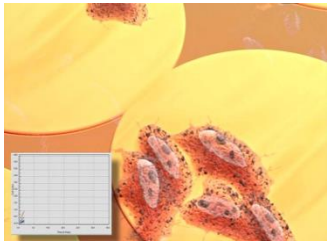
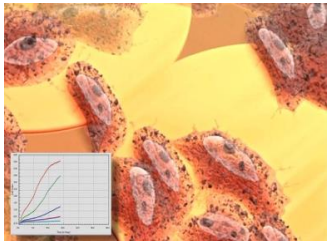
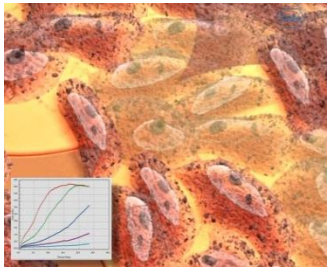
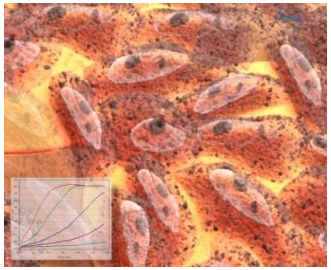


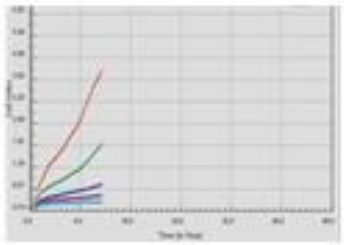
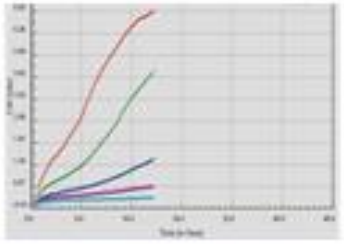
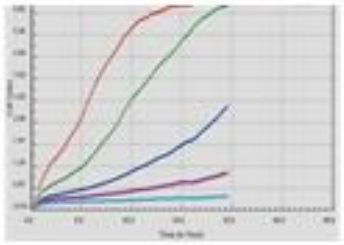
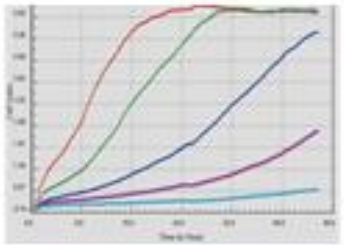
- Alternating current applied
- Impedance measured

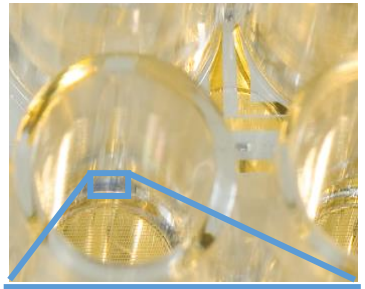
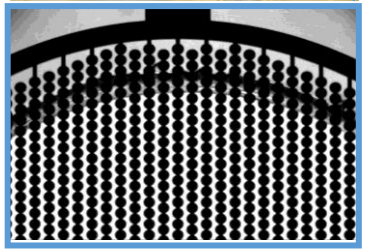
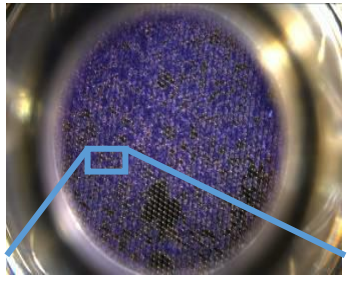
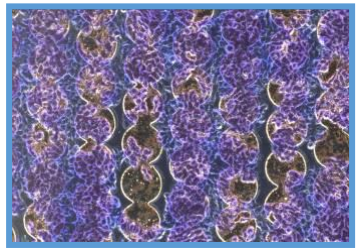


- **Label-free**
- **Real-time and kinetic readout**
- **Non-invasive, physiological measurement**

Concept: Impedance read-out

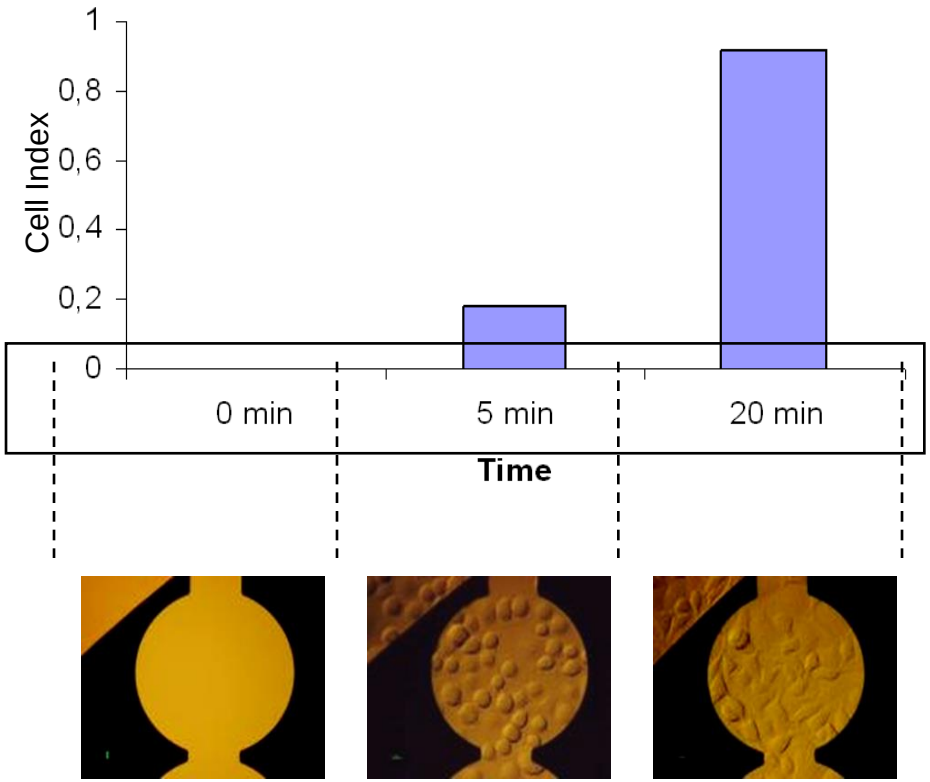





Concept: Impedance read-out

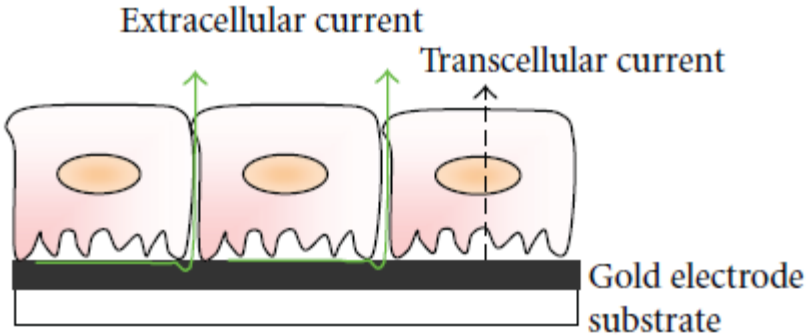
Impedance readings taken from an electronic sensor reflect changes in cellular parameters:

- **Number of cells**
- **Cell adhesion**
- **Cell size & morphology**
- **Cell viability**



Impedance Based Assays

Label free, no reporters	➢	**Disease relevant cells**
Real-time, dynamic monitoring	➢	**Kinetic and MOA information**
Continuous QC	➢	**Data quality assurance**
Non-invasive measurement	➢	**Long term / complementary**



Agenda

- Technology Concept and advantages
- **Applications**
- RTCA Software
- Key Features

Applications

- Cell Barrier function
- Cell Invasion & Migration
- Cell Proliferation
- Cellular Cardiology research
- Cytotoxicity and Cell Death
- Dermatology
- Immunology
- Microbiology, Virology, Parasitology
- Neurobiology
- Others

xCELLigence portfolio

RTCA S16

1x16

E-plate 16

RTCA DP

3x16

CIM-plate

E-plate 16

RTCA SP

RTCA Cardio

E-Plate96

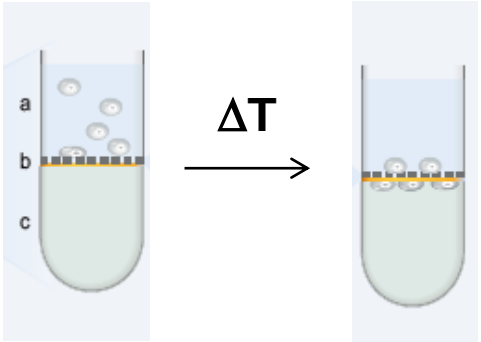
xCELLigence portfolio

RTCA MP
6x96

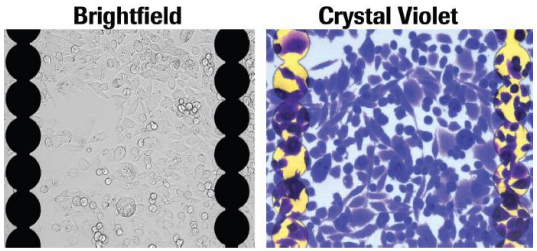
RTCA HT
4x384

Specialized xCELLigence devices

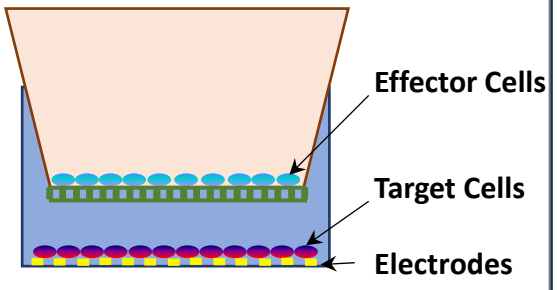
CIM (invasion/migration)



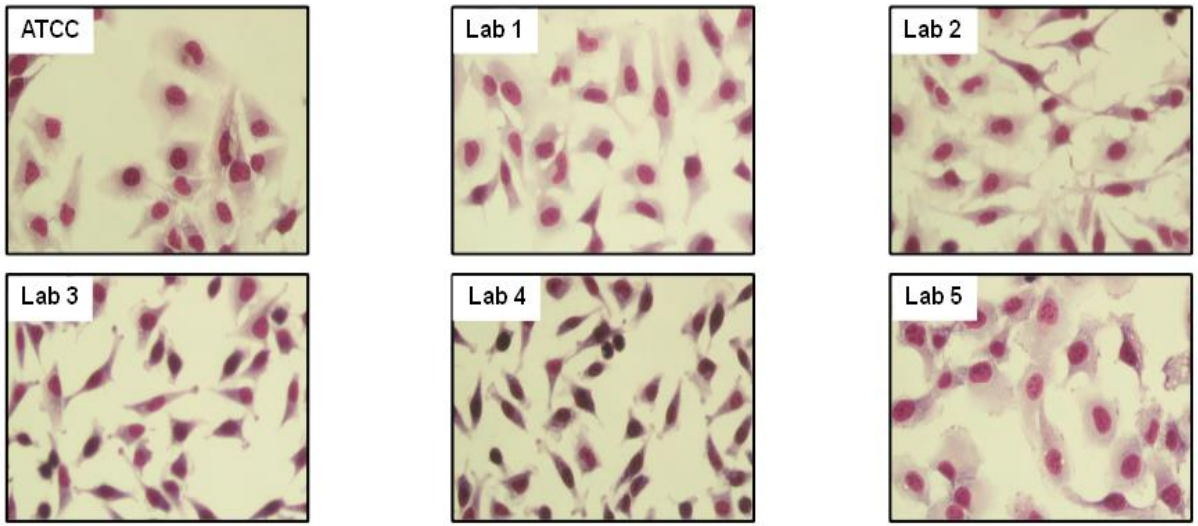
E-plate view (microscopy)

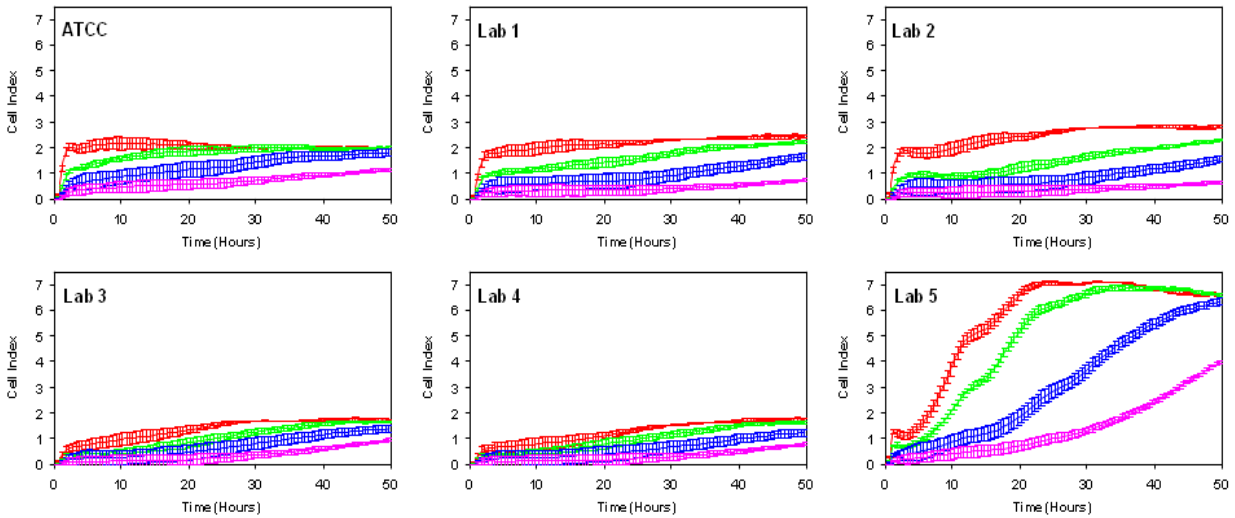


E-plate insert (coculture)



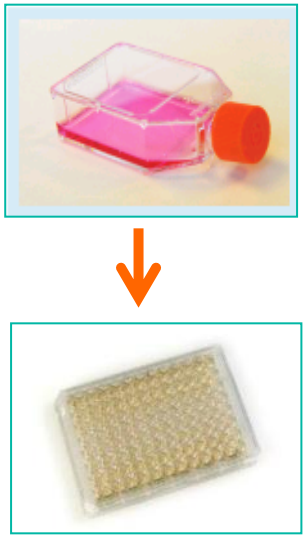
Cell quality control





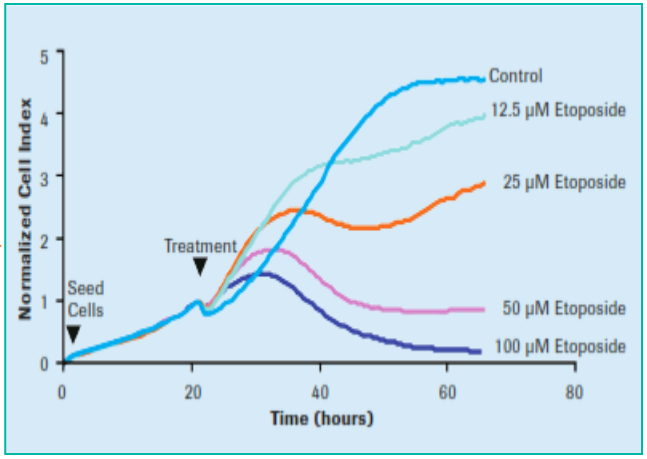
J Biomol Screen March 2011 16: 313-322.

Simple workflow



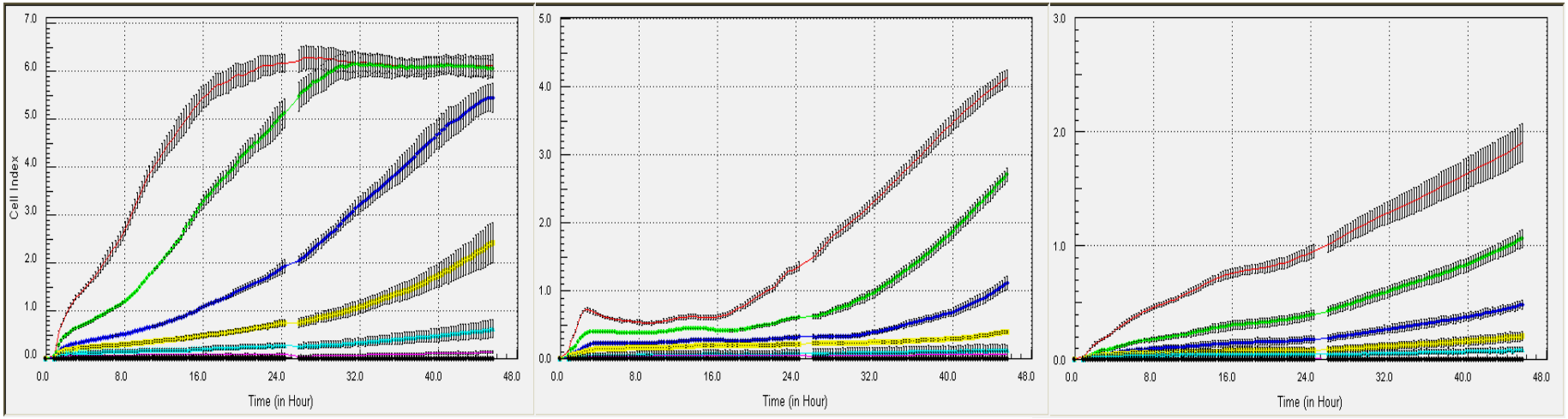
Seed Cells

Real-time monitoring at physiological conditions



Kinetic cell response curve

Basic cell Titration – typical first experiment



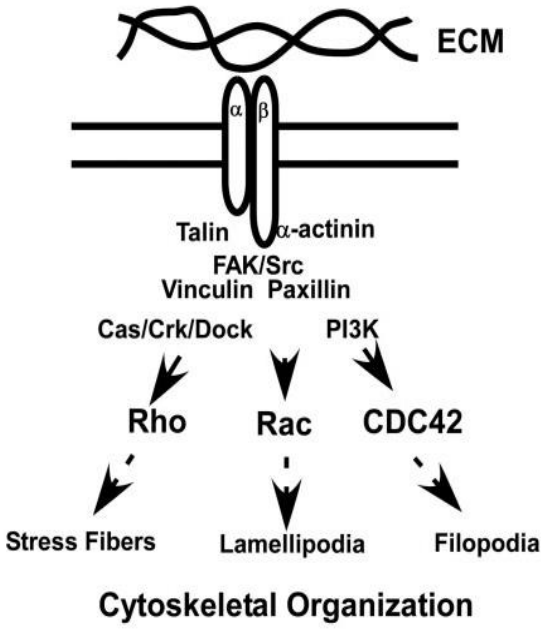
HeLa ***NIH 3T3*** ***HT29***

Red	10000 cells/well
Green	5000 cells/well
Blue	2500 cells/well
Yellow	1250 cells/well
Light blue	625 cells/well
Pink	312 cells/well
Brown	156 cells/well
Black	medium

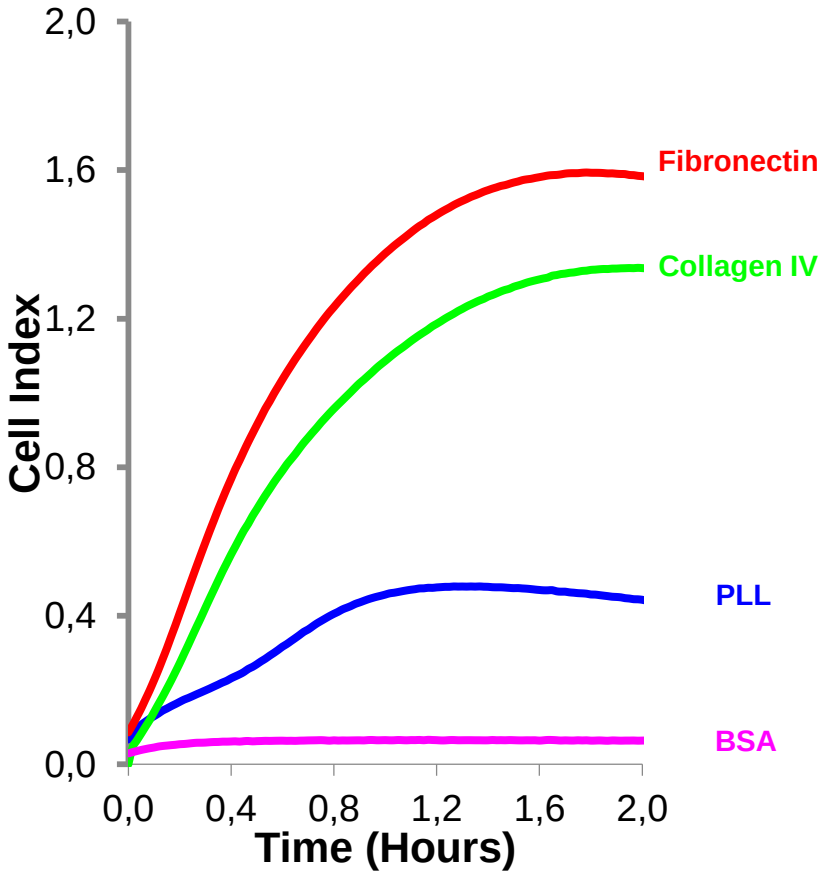
Cell lines show

- ***Different kinetic profiles***
- ***Different surface attachment***
- ***Different morphology at confluence***

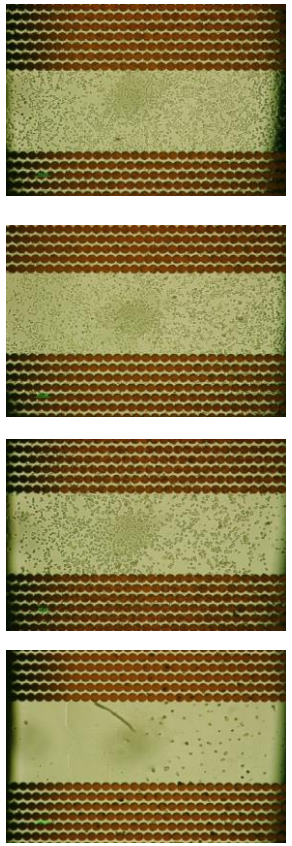
Cell Adhesion and Spreading



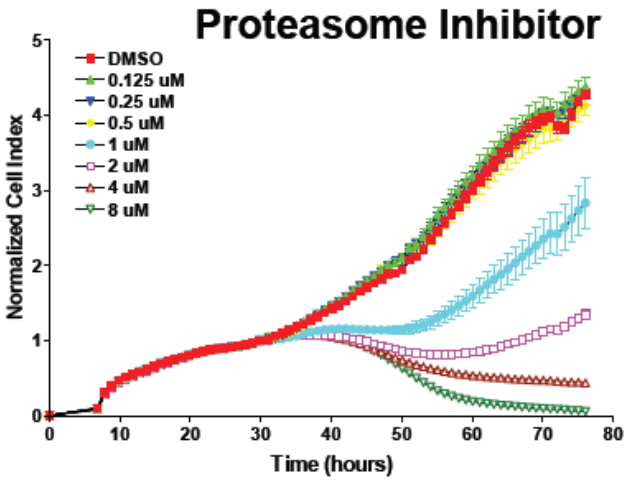
Cytoskeletal Organization

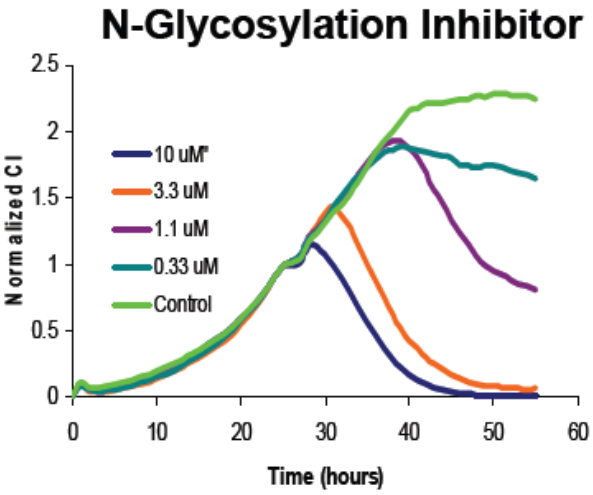


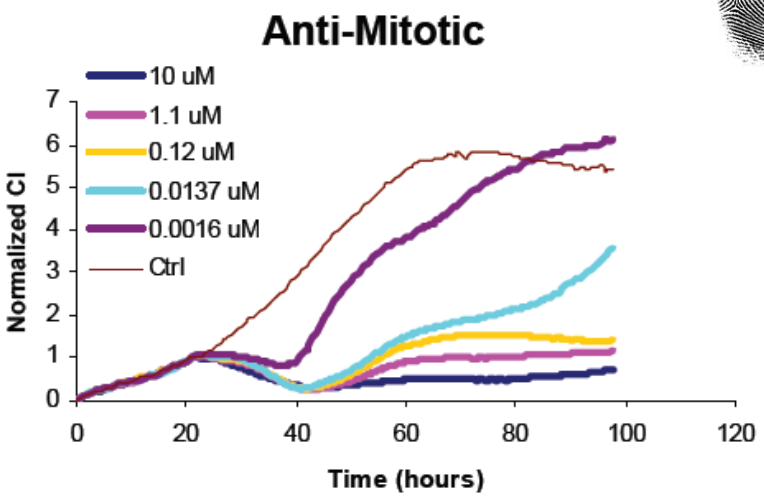
E-Plate View

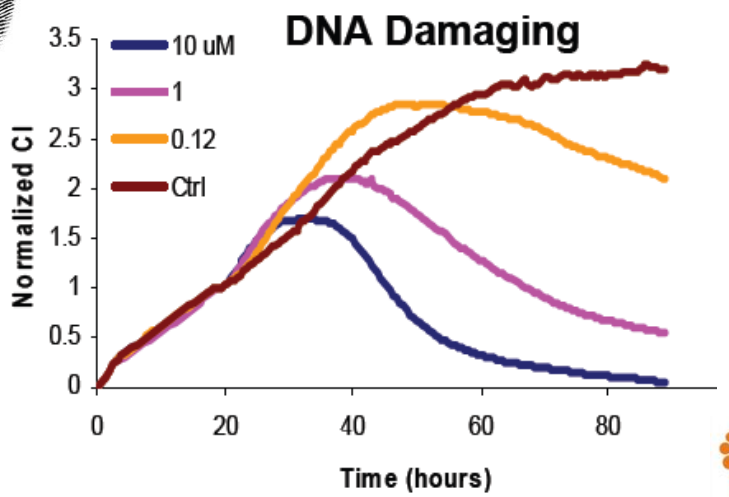


Toxicity studies

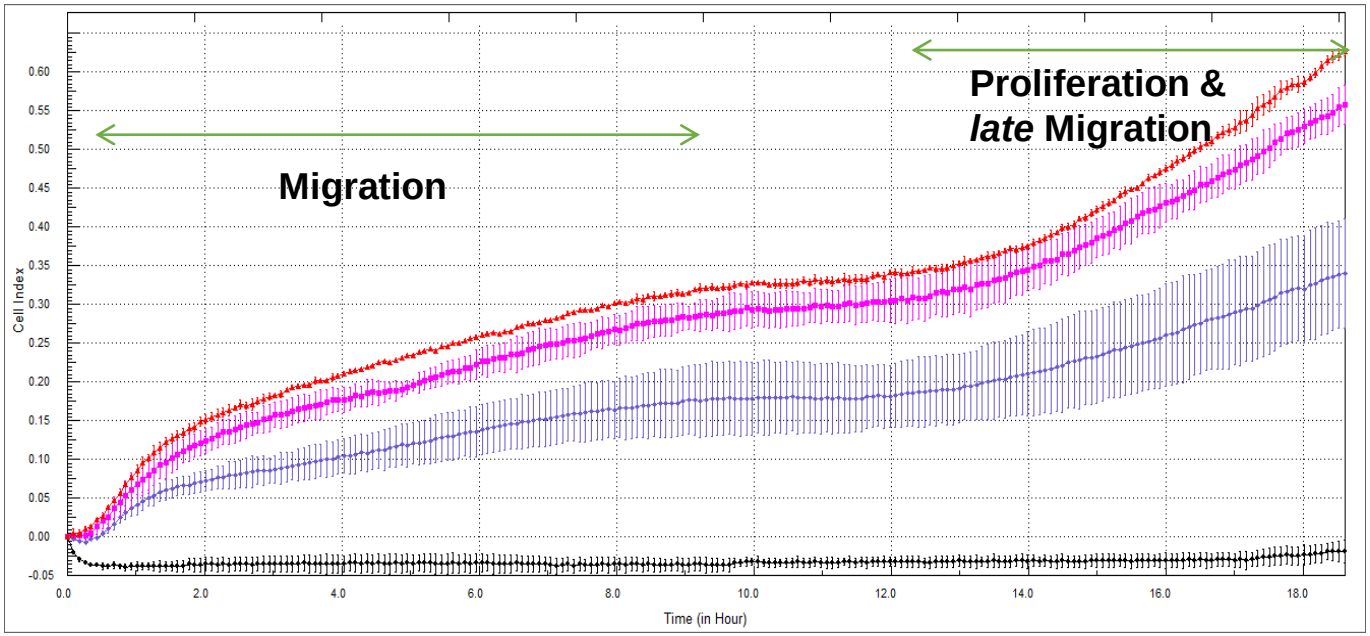








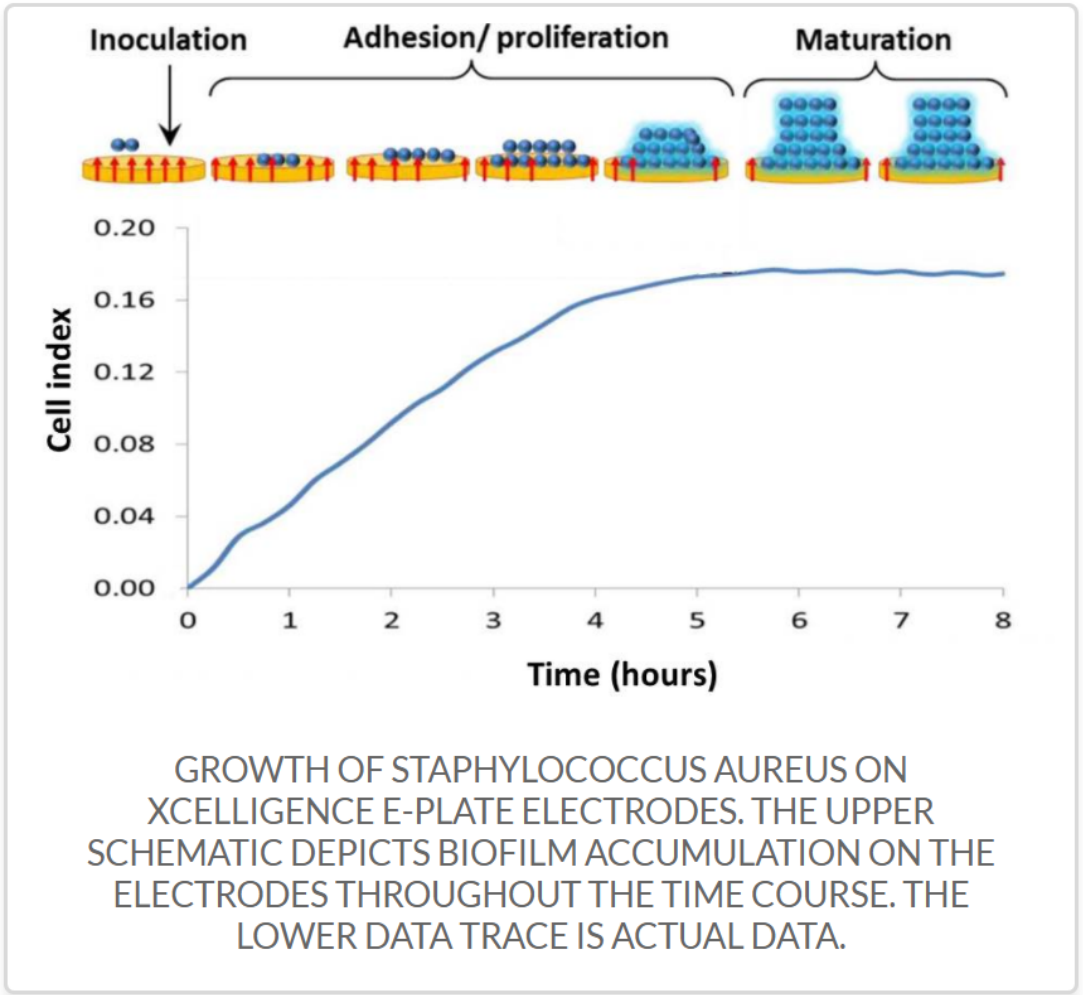
Dynamic follow-up of Migration potential



IGF – Montpellier
FRANCE

S. Aureus biofilm monitoring

Spanish scientists demonstrate that the growth and destruction of medically important bacterial biofilms can be quantitatively monitored in real-time using the xCELLigence technology

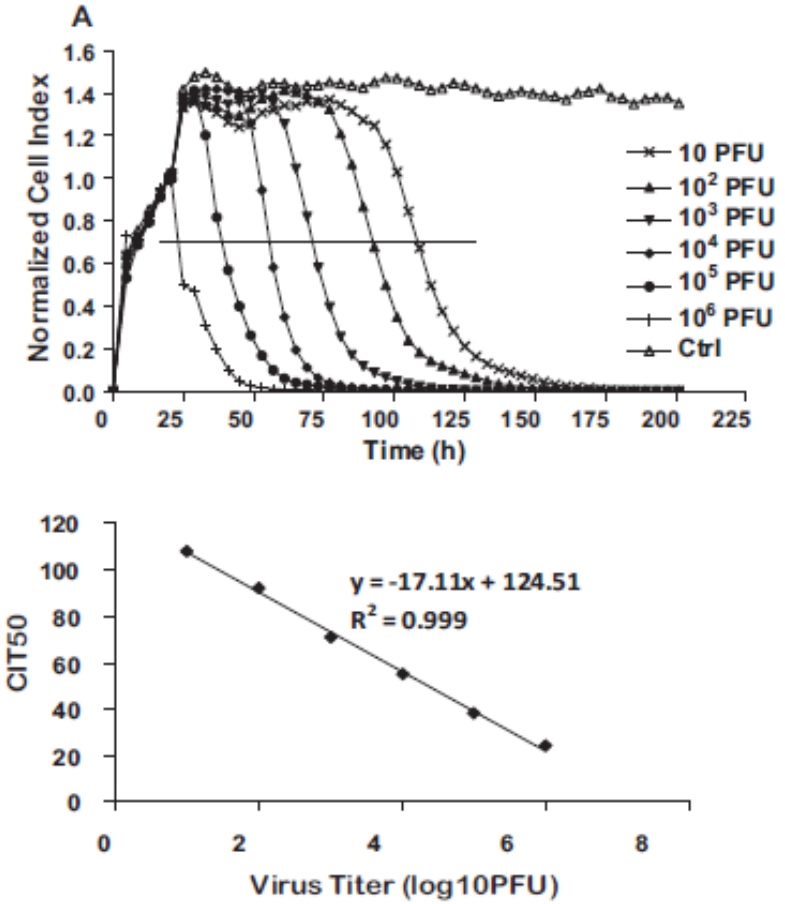


GROWTH OF STAPHYLOCOCCUS AUREUS ON XCELLIGENCE E-PLATE ELECTRODES. THE UPPER SCHEMATIC DEPICTS BIOFILM ACCUMULATION ON THE ELECTRODES THROUGHOUT THE TIME COURSE. THE LOWER DATA TRACE IS ACTUAL DATA.

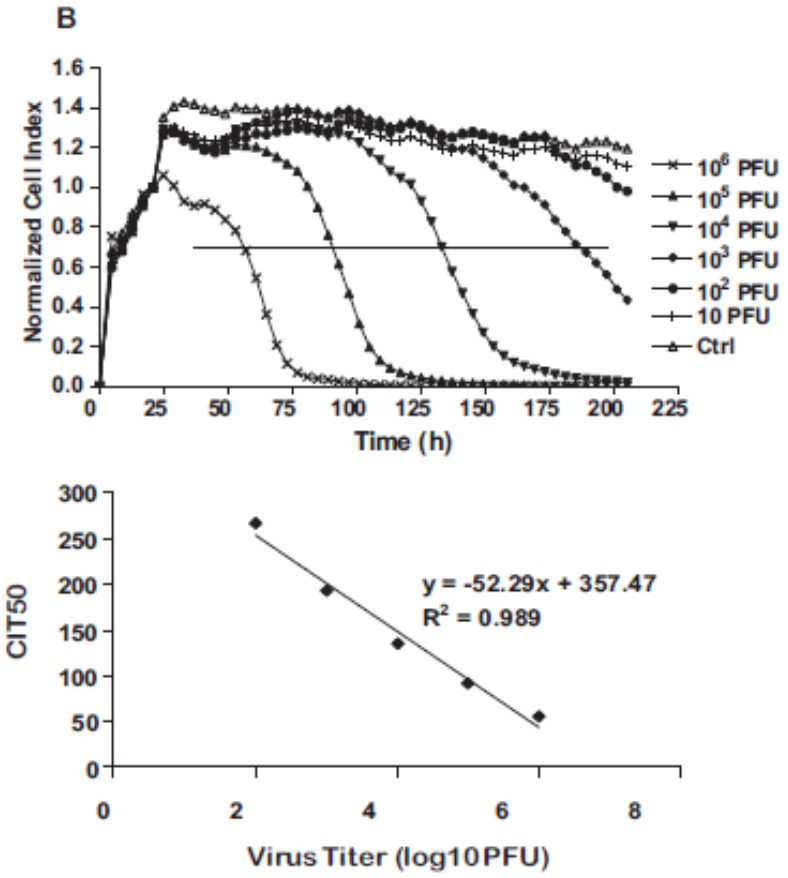
Monitoring in Real Time the Formation and Removal of Biofilms from Clinical Related Pathogens Using an Impedance-Based Technology. Gutiérrez D[1], Hidalgo-Cantabrana C[1], Rodríguez A[1], García P[1], Ruas-Madiedo P[1]. University of Valencia

Quantitative detection of virus titer

WNV-induced CPE on Vero Cells

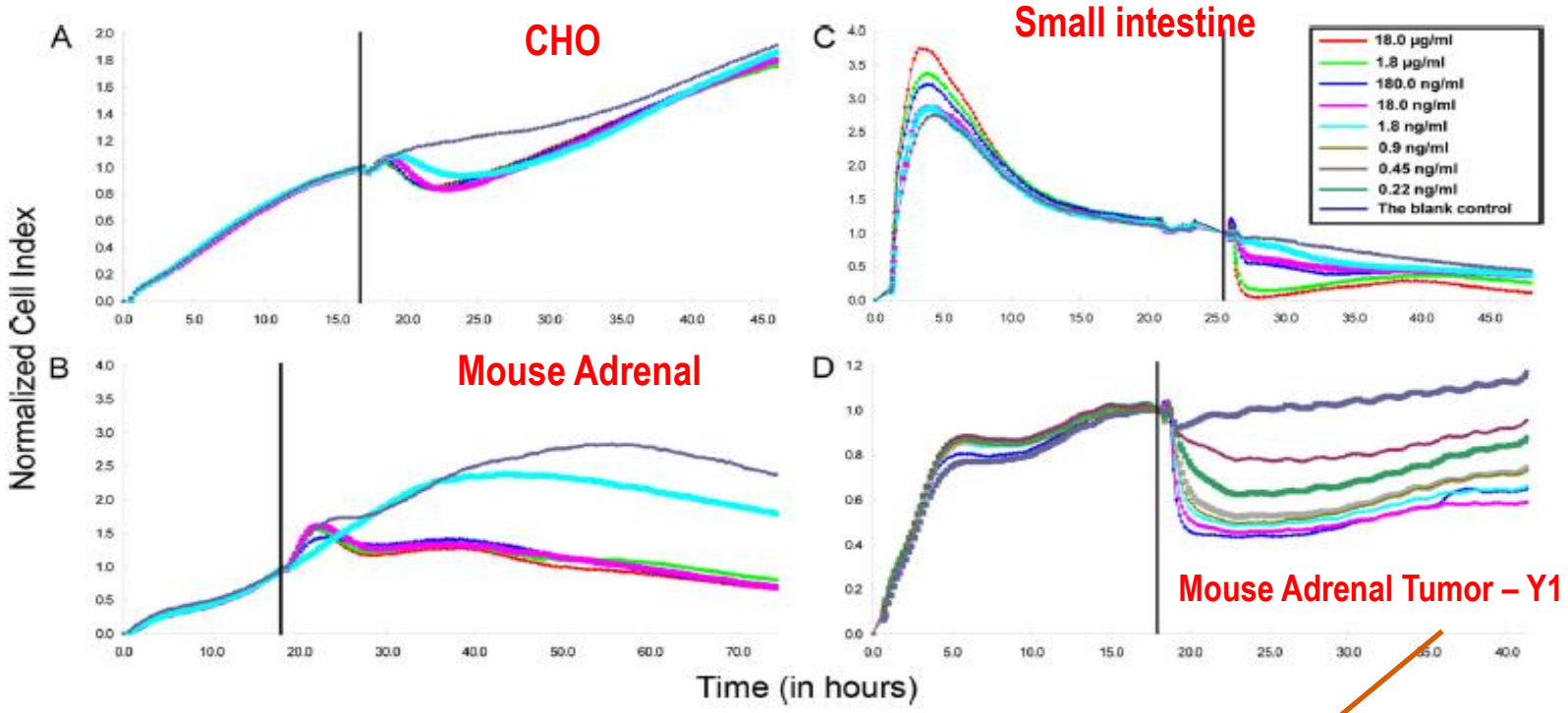


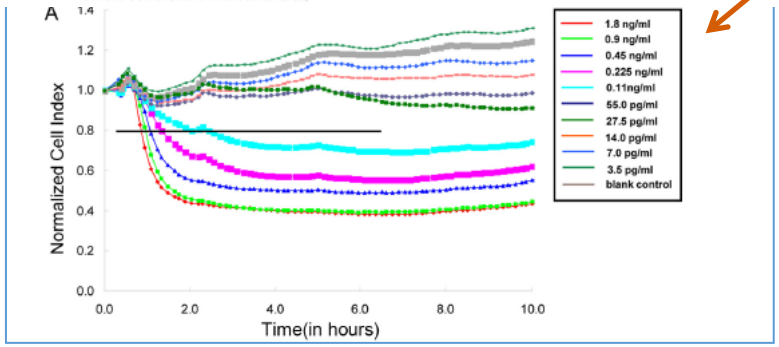
SLEV-induced CPE on Vero Cells



Journal of Virological Methods. 2011; 173: 251–258.
Real-time monitoring of flavivirus induced cytopathogenesis using cell electric impedance technology.
Fang Y, Ye P, Wang X, Xu X, Reisen W. University of California, Davis, USA

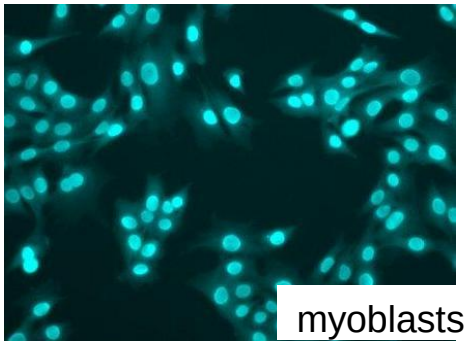
Toxicity assessment of Vibrio Cholerae toxin





J Clin Microbiol. 2013 Dec;51(12):3968-74.
Quantitative detection of Vibrio cholera toxin by real-time and dynamic cytotoxicity monitoring.
Jin D, Luo Y, Zheng M, Li H, et al., Zhejiang Provincial Center for Disease Control and Prevention, China.

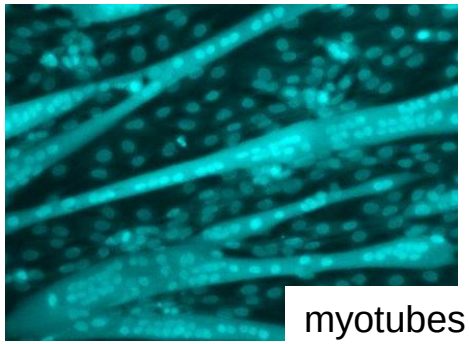
C2C12: Mouse myoblasts differentiate into muscle



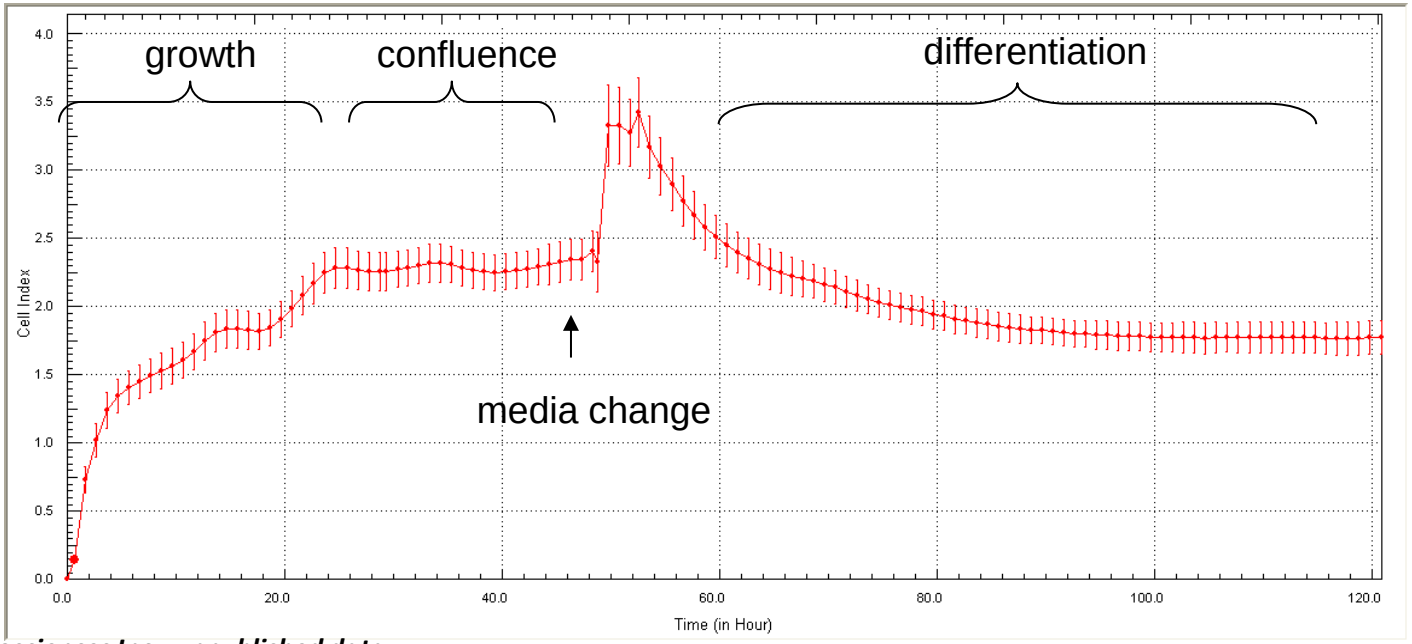
myoblasts

Confluence

Low serum



myotubes



ACEA Biosciences Inc., unpublished data

Introducing the immunotherapy kit

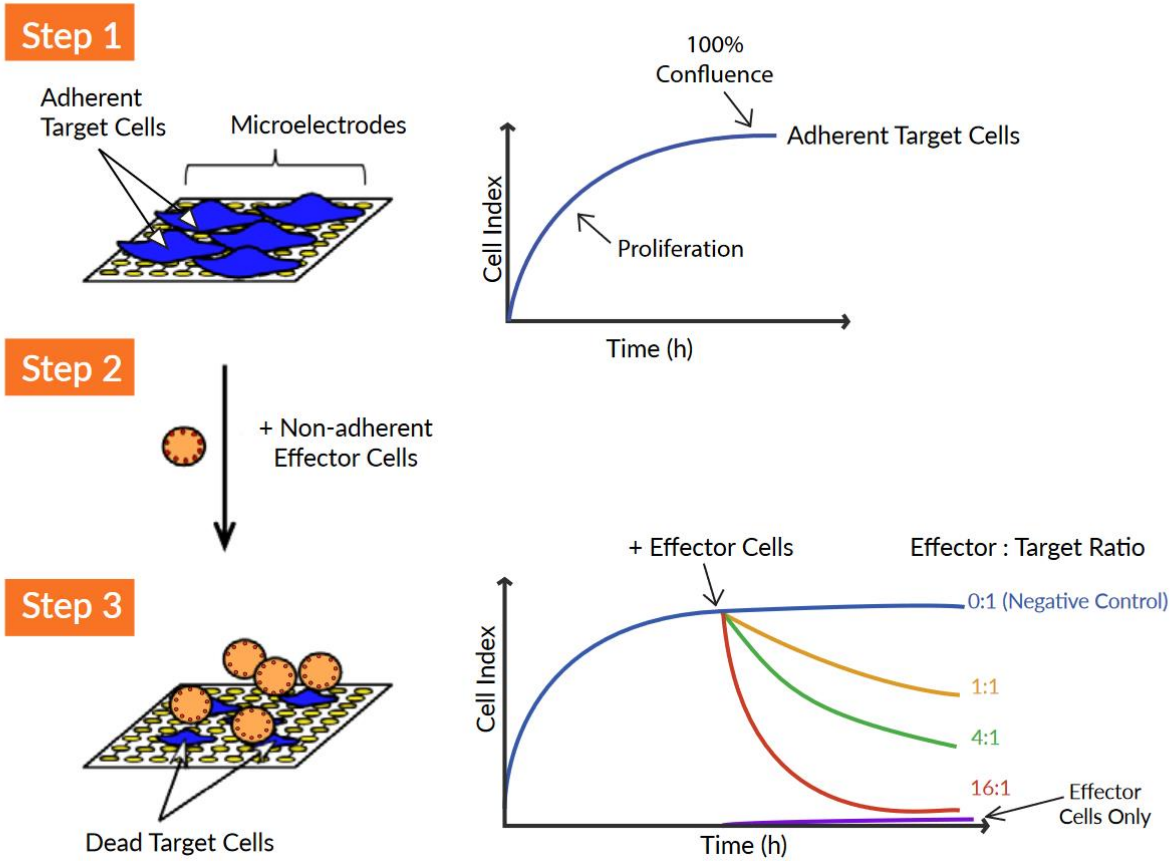
- in vitro monitoring and quantification of effector-mediated B cell killing

- continuous real-time monitoring of B cell lymphomas

Introducing the immunotherapy kit

- **B cells are selectively immobilized in the well bottoms**
- **Addition of effector cells (NK, T, CART) on top of immobilized B cells results in cytolysis of target cells.**
- **The continuous acquisition of impedance generates real-time killing curves for multiple conditions simultaneously.**

Introducing the immunotherapy kit



Anti-CD40 assay

B Cell Killing (anti-CD40) Assay

B Cell Killing (anti-CD40) **Complete Kit**	**8100004**
E-Plate View 96 (6 Plates)	
Tethering Reagent (anti-CD40)	250 µL
10X Tethering Buffer	10 mL
Cytolysis Reagent	1.5 mL
xIMT Software	

B Cell Killing (anti-CD40) **Tethering Kit**	**8100005**
Tethering Reagent (anti-CD40)	250 µL
10X Tethering Buffer	10 mL
Cytolysis Reagent	1.5 mL

B Cell Killing (anti-CD40) **Sample Kit**	**8100006**
E-Plate View 96 (2 Plates)	
Tethering Reagent (anti-CD40)	90 µL
10X Tethering Buffer	10 mL
Cytolysis Reagent	1.5 mL

*xIMT Software – one month trial version can be downloaded for free by providing the serial number of an existing xCELLigence instrument

8100004: Complete kit

8100006: Sample kit

Anti-CD40 assay

Tethering Kits: without software
- B Cell Killing (anti-CD40) (Cat# 8100005)
- Leukemic Cell Killing (anti-CD29) (Cat# 8100008)
- B Cell Killing (anti-CD19) (Cat#: 8100011)

Contains:
- 1 tube of Tethering Reagent
- 1 bottle of 10X Tethering Buffer (10 mL)
- 1 tube of Cytolysis Reagent
- xCELLigence® Immunotherapy Software 1.0
- Assay and Software Manual

For Research Use Only

Anti-CD40 assay

Cat# and Kit Components

	Catalog Number		
Products	Complete Kit	Tethering Kit	Sample Kit
B Cell Killing (anti-CD40) Assay	8100004	8100005	8100006
Leukemic Cell Killing (anti-CD29) Assay	8100007	8100008	8100009
B Cell Killing (anti-CD19) Assay	8100010	8100011	8100012

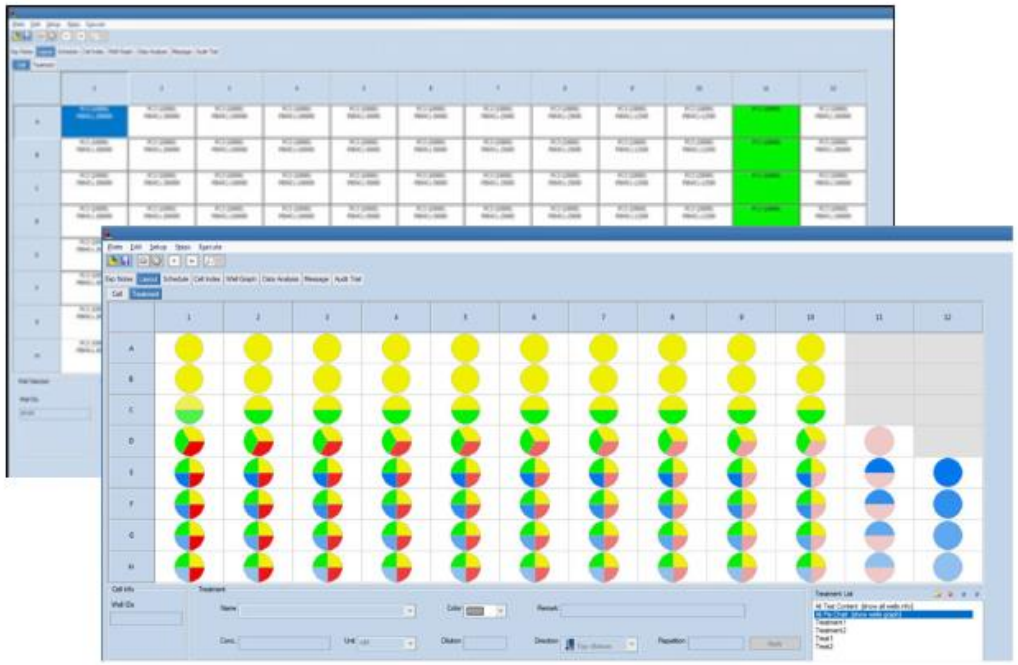
xIMT software	310100190

	Kit Components		
Contents	Complete Kit	Tethering Kit	Sample Kit
E-Plate® View 96 (1 Plate)	6	0	2
Assay-specific Tethering Reagent	for 6 plates	for 6 plates	for 2 plates
10X Tethering Buffer	√	√	√
Cytolysis Reagent	√	√	√
xIMT software	√	None	1 month usage

Agenda

- Technology Concept and advantages
- Applications
- **RTCA Software**
- Key Features

Introducing RTCA Software PRO



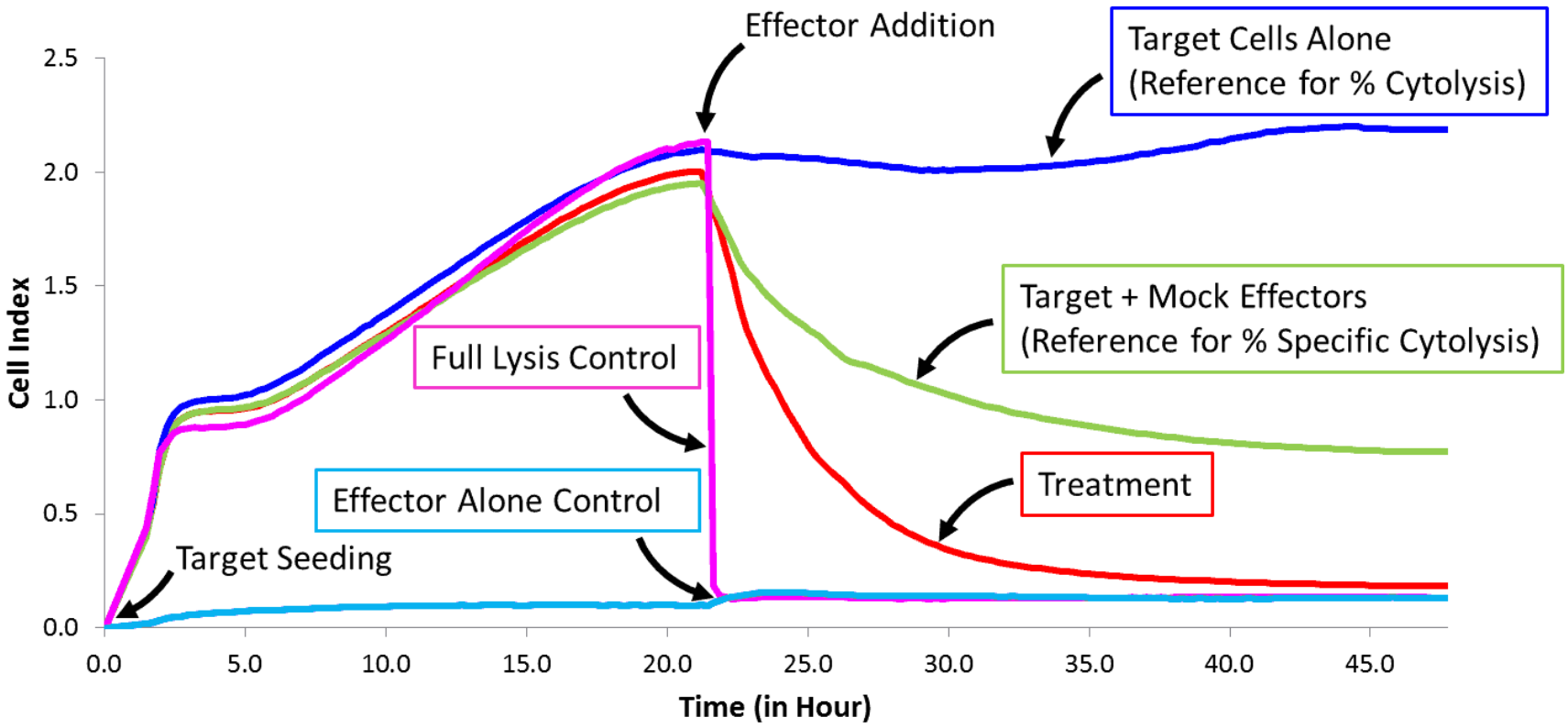
SIMPLE EXPERIMENTAL SET UP

Target cells, effectors, and treatments are easily introduced based on the experiment and well content. The interactive software interface automatically recognizes control wells based on plot type selection and normalization.

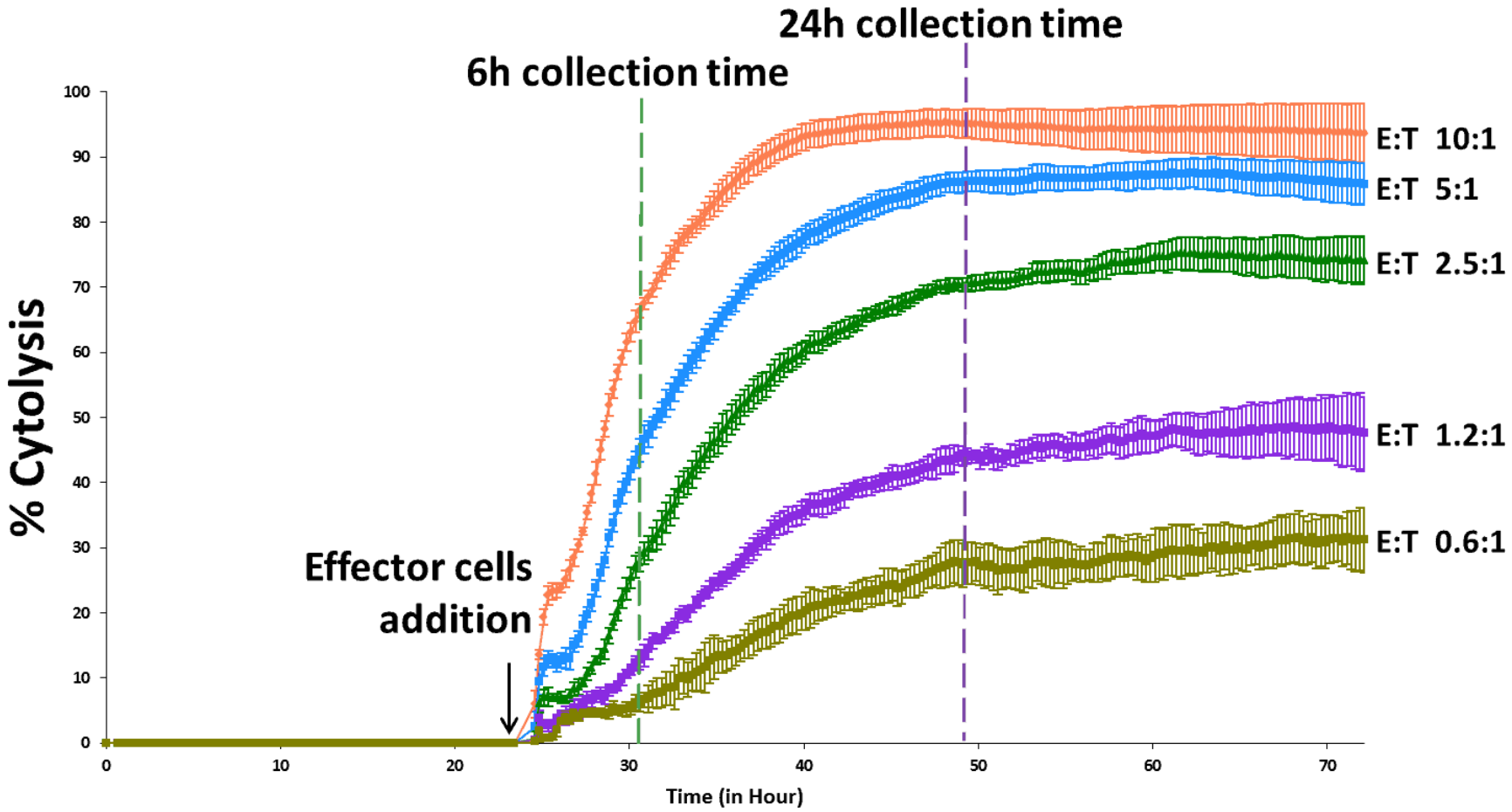
EASILY VISUALIZE WELL CONTENT

For each well, target cells, effectors, or treatments can be visualized individually or in combinations through a pie chart, enabling quick comparison between wells.

Introducing RTCA Software PRO



Accurate & reproducible cytolytic data



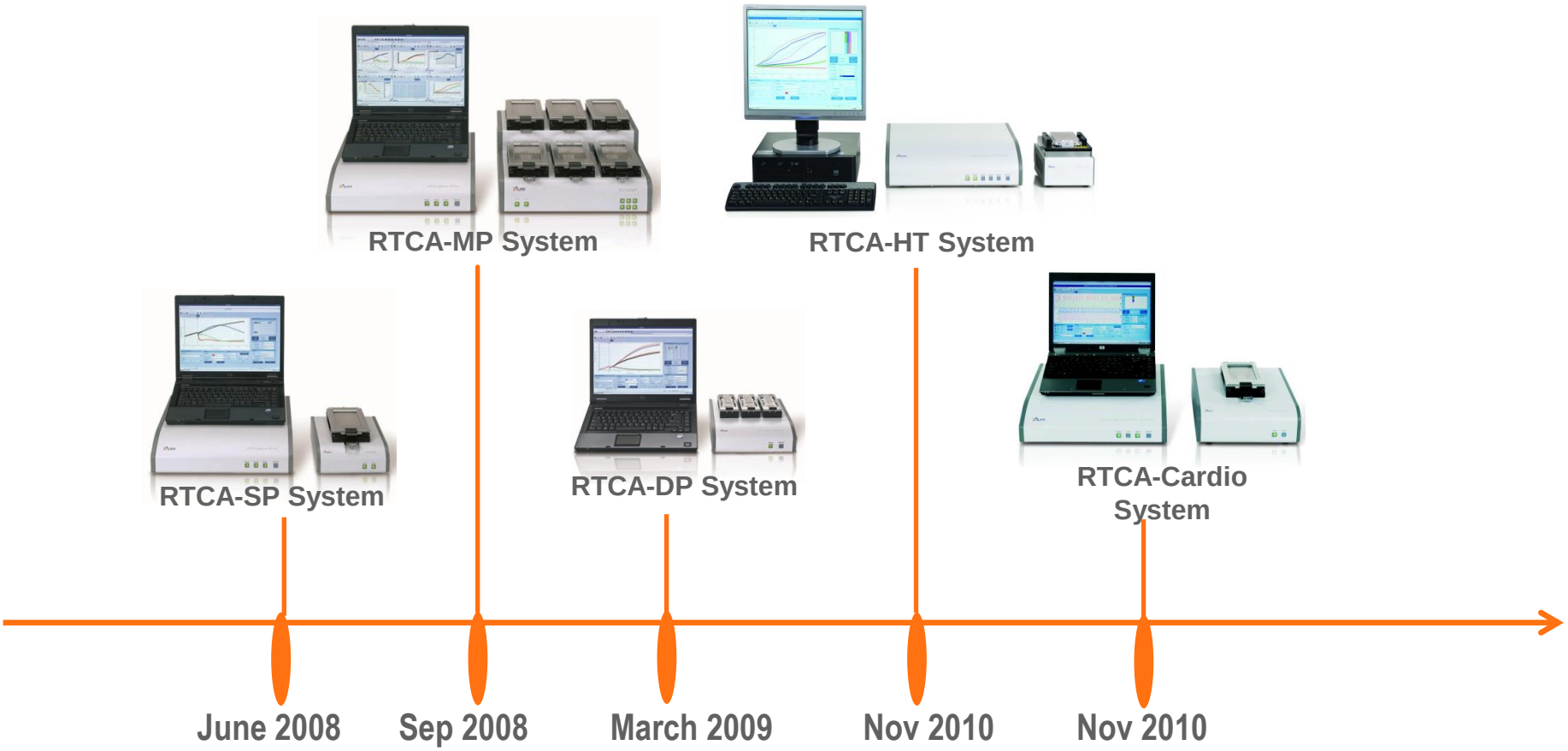
Agenda

- Technology concept and advantages
- Applications
- RTCA software
- **Key features**

xCELLigence- key features

- **Whole cellular response (early and late events).**
- **Complementary technology to traditional assay.**
- **Sensibility (low densities, weak protein expression).**
- **Quality control of the cells seeded in culture E-plates.**
- **Non-invasive assays, standardized, reproducibles.**
- **Easy to use, Wide choice of applications (customized bioassays).**

Inspired to advance your discovery



Inspired to advance your discovery

RTCA-S16

AccuWound 96

NovoCyte flow cytometer

Quanteon flow cytometer

April 2014

May 2018

May 2018

June 2018

Key resources //accela.eu

REAL-TIME, LABEL FREE CELL ANALYSIS PRODUCTS

xCELLigence DP - Acea Biosciences

xCELLigence SP - Acea Biosciences

xCELLigence MP - Acea Biosciences

xCELLigence Cardio - Acea Biosciences

THANK YOU FOR YOUR ATTENTION

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