High Content Screening and Analysis	**Category:** **A. Particle Synthesis and/or** **B. Particle Labelling and/or** **C. Particle Characterisation in and ex-situ and/or** **D. In-vitro toxicity studies** **Institute: Institute of Molecular Medicine** **Location: HCSA facilities, Room 2.28, Trinity Research Centre, St. James's street, Dublin 8, Ireland** **Contact Details of Technology Expert:** **Name: Prof. Yuri Volkov / Dr. Anthony Davies** **Phone +353 1 896 3263/2104** **Fax +353 1 4542043** **E-mail: yvolkov@tcd.ie**

Short technology description/Overview:

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The National Centre for High Content Analysis (HCA) incorporates several state of the art imaging platforms, liquid handling devices and image processing software that allow for high throughput, high content analysis of cellular interactions on both a population and individual cell level. There are a number of liquid handling platforms in the facility, which allow for rapid precision dispensing of liquids in nanolitre volumes. Cellular responses and interactions can be investigated in both live and fixed cell populations in adherent cells allowing for accurate detailed information. The high content imaging platforms offer both live cell and 3D pseudo-confocal capabilities. The image and data analysis suite comprises image processing packages are available for analysis of data.

The two GE Healthcare InCell-1000 Analysers and the Cellomics KineticScan HCS available at TCD centre open up a new scope of opportunities in multi-parameter real time molecular imaging and analysis of the chosen living cellular models. These workstations enable to minimise the use of animal at the early stage of drug discovery process such as at the selection of the new leads from the candidate compounds.

Based on the novel technological concept of high content analysis, this equipment allows performing analyses of responses in individual cells and their subpopulations in a wide range of experimental conditions using a multi-well (96 and 384 wells) format. Screening for nanoparticle-cell-interactions at the cellular level will be performed rapidly with the benefit of sequential time points using real time multi-colour imaging. The HCA systems will be of particular value for validation of cellular response to novel nanoiparticles due to its ability to account for heterogenic kinetic responses, revealing thereby complex molecular correlations that fall below detection threshold in well-average responses.

Therefore, HCA is a key enabling facility associated with scaling-up processes where multiple nanomaterial leads will have to be screened in multiple cell types to identify suitable hits.

Main Features (Equipment Capabilities): (in green the one we declared)

- GE Healthcare InCell Analysers, for high throughput capability (equipped with multiplates robot loader)

  Multiple plates loading (up to 80 plates robot loader)

  High magnification (4, 10, 20 optical magnification in plastic)

  Compatible with 96, 384 commercially available plastic plate well (Nunc, etc)

- GE Healthcare InCell Analysers, for confocal capability

  Single plate load

  CO2, temperature and HR controlled incubation

  High magnification (10, 20, 40 optical magnification in plastic and glass substrates)

  Low volume incubation in commercially available cell culture glass slide chamber

- Cellomics KineticScan HCS

  Single plate load

  CO2, temperature and HR controlled incubation

  8 channel microlitre automated injection for multi compound screening

  Digital Magnification (plastic and glass substrates)

  Cellomics Pattern recognition software for morphological and fluorescent imaging

- Deerac Fluidics/Matrix liquid handling systems designed for precision nanomaterials dispensing

- Matrix-Well liquid handling (automated)

  8 channel injection system

  Adjustable injection volume (10ul – 1ml)

  Multiple/programmable liquid handling

Typical Samples & Images:

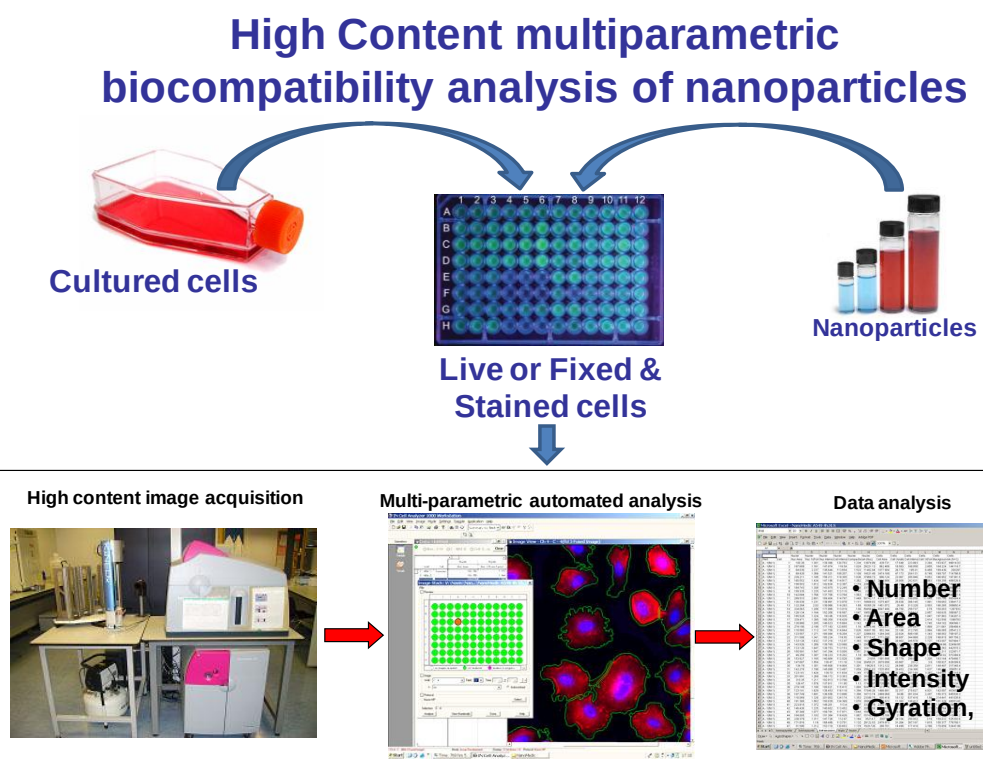

Figure 1 – Schematic representation of High Content experimental design and workflow (courtesy of Dr. Verma)

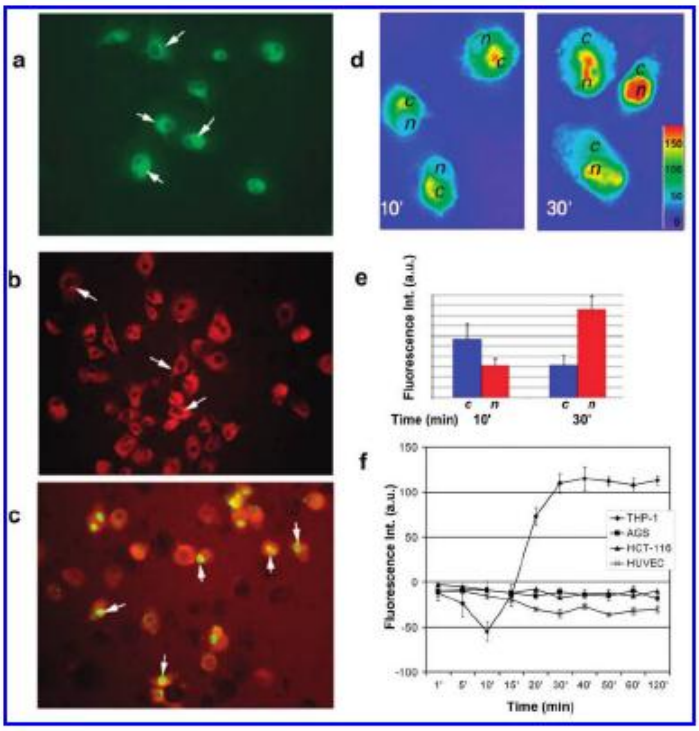

Figure 2 - Intracellular localization of green (2.1 nm) and red (3.4 nm) CdTe QDs in the macrophage-like THP-1 cell line and epithelial cells. (a) Early stage green CdTe QD accumulation in THP-1 cells. (work carried out at IMM HCSA facility, at Volkov's Nanomedicine and Molecular Imaging Laboratory and published in Nano Letters, 2007)

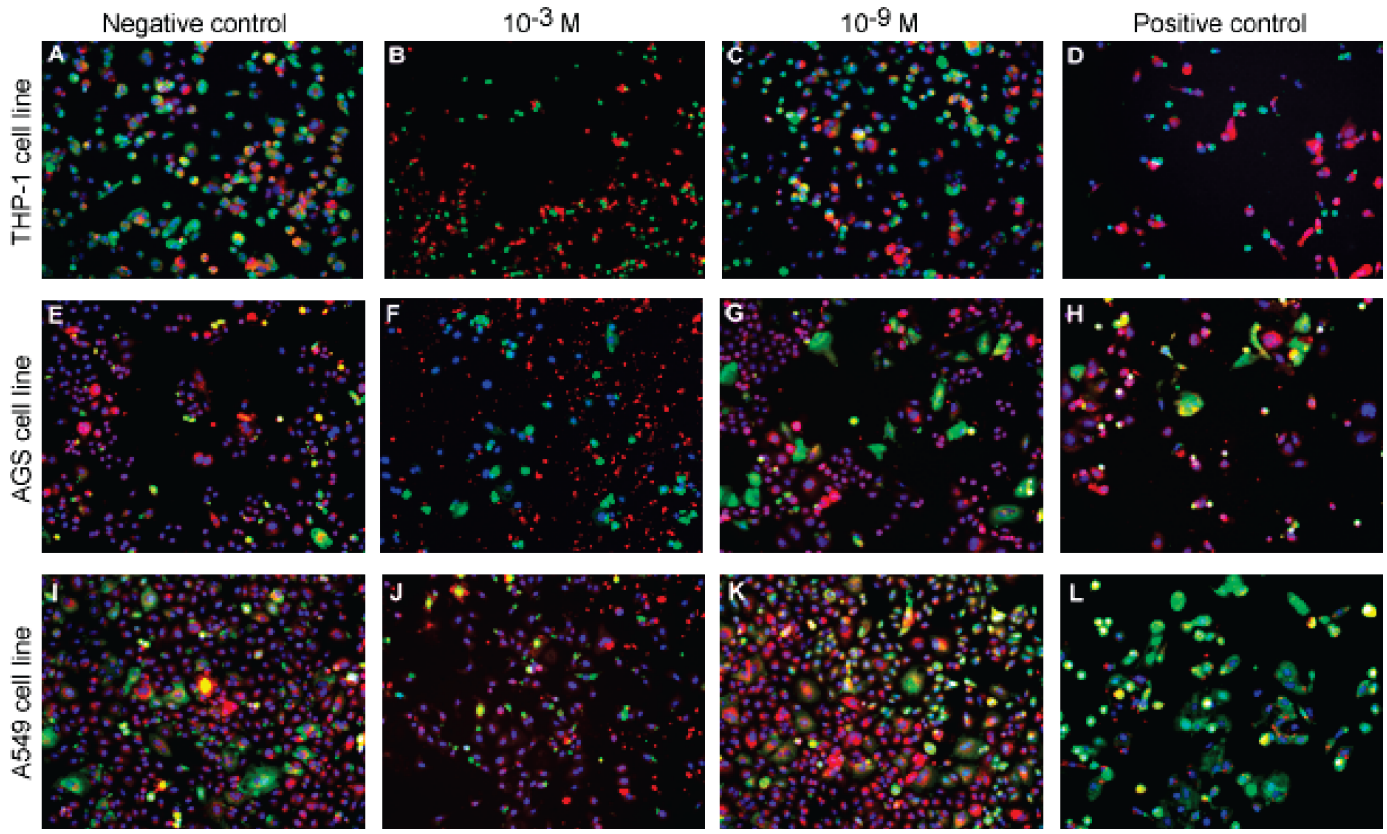

Figure 3 - HCSA qualitative results for THP-1, AGS cells, and A549 cells at 24 h of exposure to the spiropyran molecules. (work carried out at IMM HCSA facility, at Volkov's Nanomedicine and Molecular Imaging Laboratory and published in Chem. Res. Tox. 2010)

Any further Information: