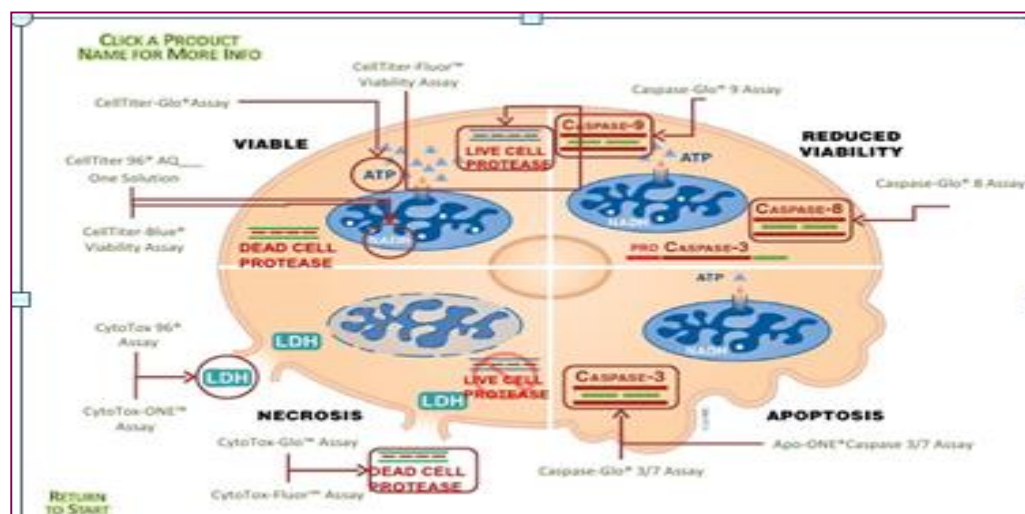


# Screening for Cell Death

## A Comparison of Methods



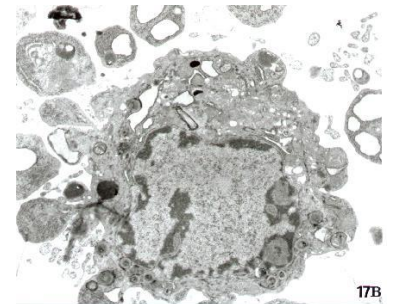
Lisa McWilliams,  
HTS, Discovery Sciences, AstraZeneca;  
ELRIG Research and Innovation 2015  
18/03/2015

# Importance of cytotoxicity screening

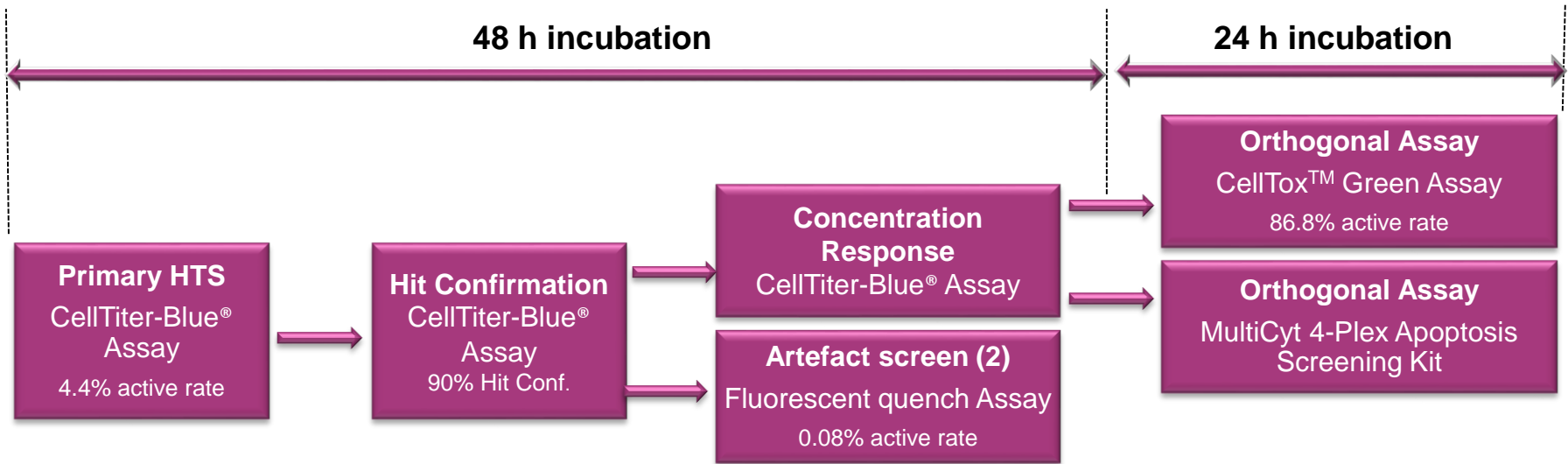
**Within AstraZeneca we are performing an increasing number of cell based assays where cell toxicity can be a confounding activity**

**Cell-based screening now accounts for about half of all HTS screens carried out in AstraZeneca.**

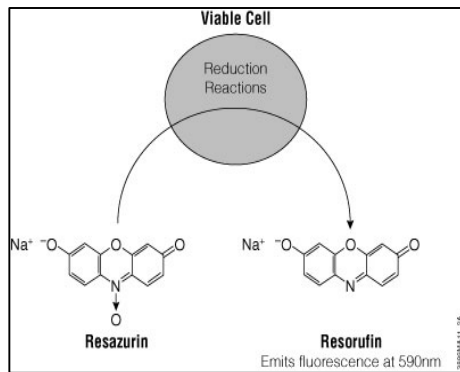
**Toxicity is also a key reason for failure in the clinic and it is desirable to annotate clusters from HTS screens to alert projects as to which clusters may have a toxic liability.**



# Screening cascade

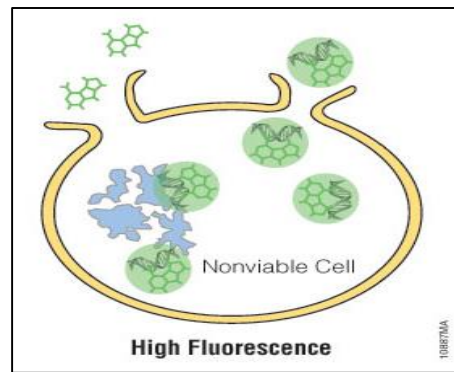


Promega  
CellTiter-Blue®



**Cell Viability**

Promega  
CellTox™ Green



**Cytotoxicity**

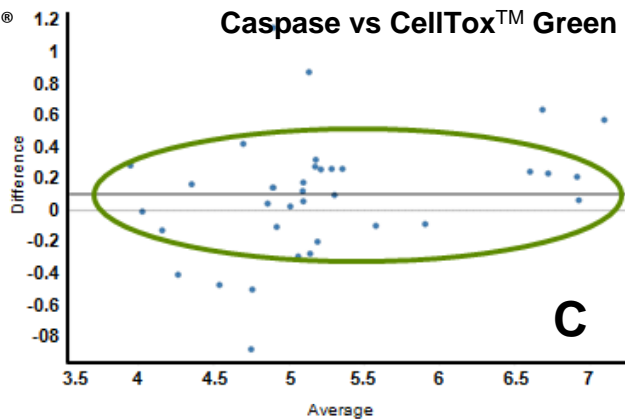
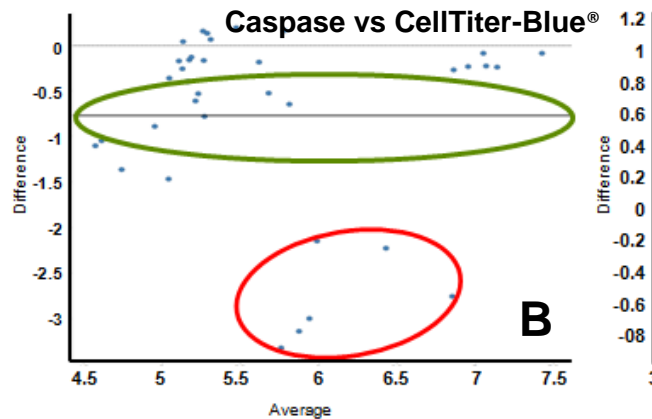
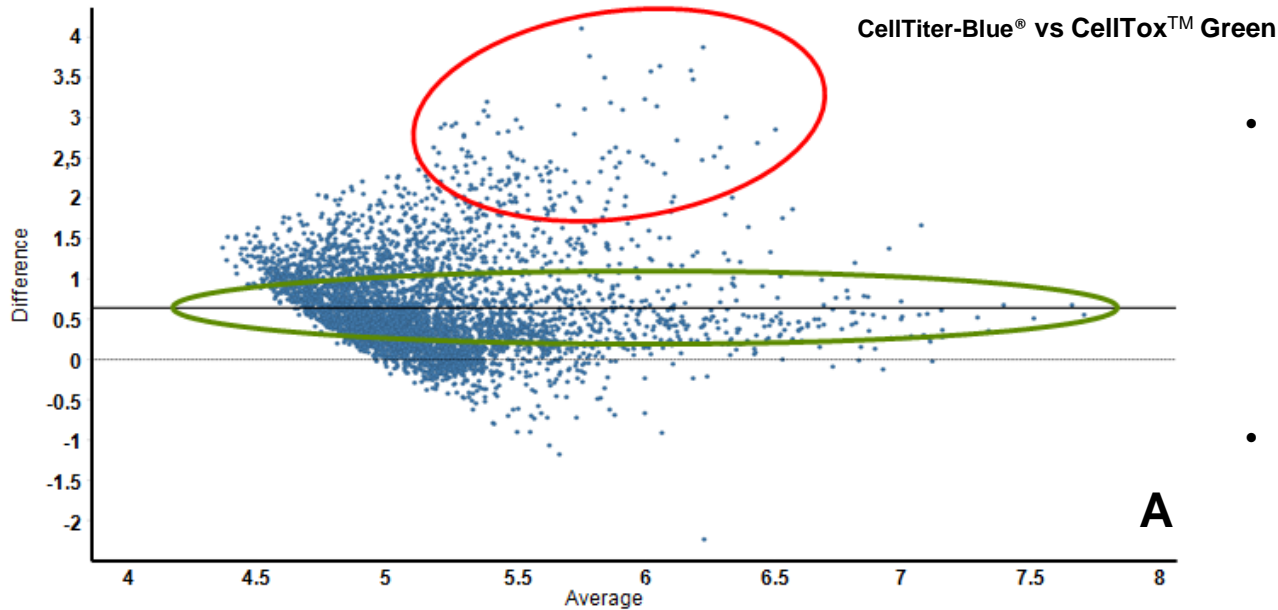
Intellicyt iQue platform  
Multicyt Apoptosis kit



**Apoptosis**



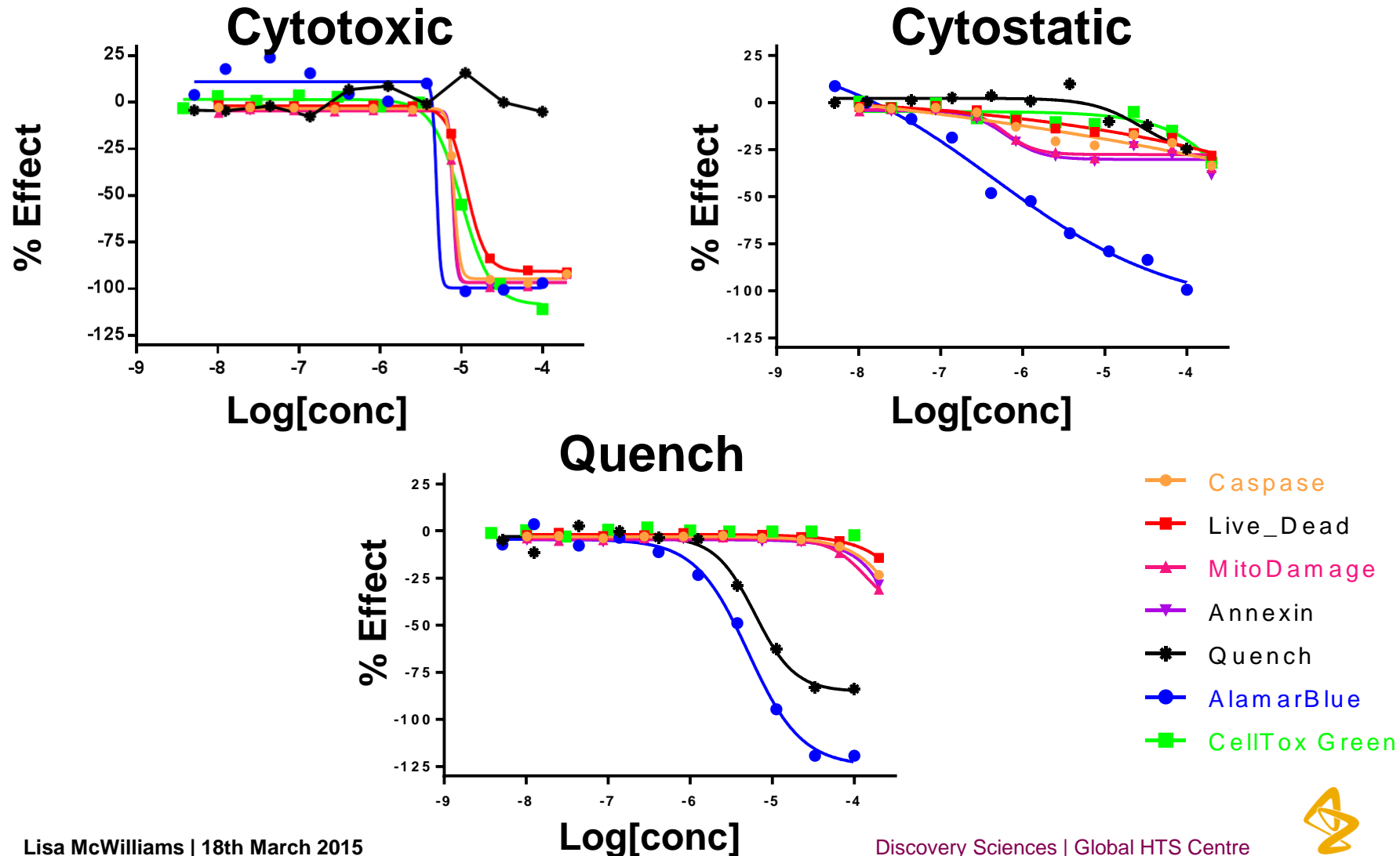
# Assessing agreement of different assays



- Group of compounds (red circle in graph A and B) showing higher potency when cell viability measured by CellTiter-Blue® compared with other cytotoxicity assays
- Difference seen may be due to cytostatic activity of these compounds
- Data in graph C show that there is good agreement between a measure of membrane integrity (CellTox™ Green) and markers of apoptosis (flow cytometry 4-plex assay).



# Use of multiple methods leads to more reliable assessment of compound toxicity



# Further annotation is essential

**CellTiter Blue® assay results in a significant number of potential false positives and should not be used in isolation to determine cell toxicity.**

**It is recommended that a measure of membrane integrity is used routinely as it appears more reliable to assess compound toxicity.**

**We anticipate that this annotation of our screening collection will allow better decision making early in cascades especially where cellular screening systems are used.**

