highly valuable and reproducible results but also led to continuous rise in both basic and applied cell-based research activities. The 1960s experienced an accelerated increase and rapid diversification in the field based on major achievements in the culturing of cells with finite life span, the development of tumour-derived immortalised cell lines as well as rapid progress in mass cell production and storage. A decade later, the introduction of cell fusion and recombinant DNA technologies along with the widespread use of the first high-density, cell culture and assay formats[2] firmly established the central role of cell-based research and in vitro assays in both academia and industry.[3] As a major consequence of this development, the 1980s and 1990s experienced almost exponentially growing research activities relying on cell-based, in vitro assays. Because of this more and more complex scientific and challenging numeric throughput, goals came into reach, generating the need to further miniaturise and automate the cell-culturing methods and cell-based assay techniques as well as the demand for intensified interdisciplinary scientific exchange. This trend became the major driving force for the implementation of high-throughput experimentation and screening approaches in pharmaceutical drug research[4] and academic probe development.[5] Most of the underlying concepts and strategies, workflows and core-technology platforms reached maturity shortly after the turn of the millennium. By now, their impact is widely proven and accepted with cell-based in vitro assays comprising roughly half of the screening and research activities – something that would not have been possible without employing high-density plate microplate formats (i.e. 96, 384 and 1536 well).

2 Scaling Down to Optimally Implement Robust and Reliable Test Systems

However, miniaturisation in cell-based assay development isn't primarily about increasing the number of assay points per se or cost reduction due to lower reagent consumption, although both aspects do represent major benefits and driving forces (see Table 1). In fact, opting for a miniaturised assay protocol in the first place

[2] That is, the 96-well plate described by Gyula Takátsy in 1951 already

[3] Aside from the growing public debate over the disproportionate use of experimental animals in certain research areas

[4] See: Foundation of the Society for Biomolecular Sciences (SBS) in 1994 (http://www.slas.org/about/who-we-are/society-for-biomolecular-sciences/) now an integral part of the Society for Laboratory Automation and Screening (SLAS) established in 2010 (https://www.slas.org/).

[5] As exemplified by the foundation of (a) the NIH Chemical Genomic Center (NCGC) in 2004, now a part of the National Center For Advancing Translational Science (NCATS; established 2012; http://www.ncats.nih.gov/research/reengineering/ncgc/ncgc.html) or (b) the Innovative Medicines Initiative (IMI; http://www.imi.europa.eu/content/home) established in 2008 as well as (c) the establishment of the National Cancer Institute Chemical Genomics Consortium in 2009 (http://dctd.cancer.gov/CurrentResearch/cbc/20090810_meeting.htm)