NEW FLASH IMAGERS facilitating higher throughput functional GPCR assays!

The recent availability of tailored automation solutions that combine liquid handling at the reading position with the latest innovations in low light imaging technology are providing screeners with new tools for the measurement of high throughput flash luminescence. These systems are proving particularly suited to the study of GPCR activation, using photoproteins such as aequorin as indicators of intracellular calcium. This article reviews the advantages of aequorin flash luminescence, compares the latest detection instrumentation, discusses the availability of new aequorin-based assay services and highlights the development of several new and improved photoproteins that have potential in the detection of calcium release triggered by several receptors.

By Dr John Comley

G protein-coupled receptors (GPCRs) have been and look set to continue to be one of the most important target classes in the portfolio of the majority of pharma and this reflects the fact that recent experience has shown them to be highly druggable targets. Upon binding of agonists GPCRs that couple to a member of the Gq/11-protein family of seven transmembrane (7TM) receptors activate PLC (phospholipase) which leads to a rapid and transient increase in intracellular calcium concentration. The peak increase in calcium concentration, which occurs within five to 10 seconds and usually returns to basal within 30 seconds to one minute following agonist addition, is used to monitor GPCR activation. The development of molecular strategies for the coupling of the majority of GPCRs (non-Gq 7TM receptors when co-expressed with promiscuous or chimeric G proteins) to calcium signalling has opened the way for the development of a generic platform for high throughput GPCR functional screening. Methodologies for the measurement of intracellular calcium have predominantly been based on fluorescent calcium dyes such as Fluor-3. However the use of cell lines co-expressing a GPCR and the photoprotein aequorin provides for a robust alternative generic assay based on light emission (flash luminescence). The apo-enzyme (apoaequorin) needs a prosthetic group (coelenterazine) to be converted to aequorin which is the active enzyme. Upon calcium binding, aequorin oxidises coelenterazine into coelenteramide with the production of CO₂ and the emission of a blue light flash (see Figure 1). Measurement of light emitted provides a reliable tool for intracellular calcium concentration (aequorin's micromolar affinity for calcium (Kd=10µM) makes it a good sensor in the biological range) and gives results comparable to those determined using fluorescent dyes. The main downsides to established fluorescent approaches are the costs associated with running these assays (dye, cell culture, poly-D-lysine coated plates and labour), the assays generally require an adherent monolayer of cells and the protocols are complex.
(usually involving multiple steps and cell washing). The potential benefits of aequorin flash luminescence assays over fluorescence methodologies for the screening for GPCR activation are numerous (see Table 1).

**Why is aequorin use limited?**

With the clear benefits associated with aequorin as a generic screening platform for calcium mobilisation assays it is somewhat surprising that adoption to date has been rather limited. Around 10% of all GPCR activation assays are estimated to been done by aequorin flash luminescence today. This relatively low uptake of aequorin can probably be accounted for by several reasons. First, many potential users have already invested heavily in the FLIPR® system and have established familiarity, expertise and have validated pharmacology and procedures with fluorescence-based assays. The availability of the no-wash FLIPR® Calcium 3 Assay Kit from Molecular Devices effectively removed many of the perceived obstacles (low throughput, dye loading and cell washing) associated with other fluorescence-based approaches, although most protocols still rely on plating adherent cells. Clearly, many of these FLIPR® users would find it difficult to change to an aequorin alternative if it required major capital investment in a new detection instrument. Second, for quite some time the patent situation surrounding the use of aequorin in cellular assays was unclear, although with Euroscreen’s exclusive licence to the University Of Georgia Research Foundation’s patents their strong worldwide IP position is now recognised. Under the patented technology platform name AequoScreen™, Euroscreen now markets the use of aequorin technology and recombinant cell lines that express apoaequorin. The use of apoaequorin-transfected cell lines in screening and the addition of such cell suspensions to compounds during automated assay protocols are both protected by Euroscreen patents. Previously Euroscreen’s licensing terms for aequorin were regarded by some in the pharma industry as an obstacle to its adoption, particularly as a significant number of companies had independently developed in-house expertise with aequorin biology. However, the current licensing terms, which have been in effect for about a year, have been better received and enable collaboration partners to
either purchase specific AequoScreen™ cell lines, calcium optimised cell lines, GPCR antibodies, assay design, natural ligands or internal HTS services for a price that now incorporates patent considerations. Alternatively, a partner can purchase an annual licence which gives full flexibility to the partner to transfect its own cells. A significant incentive now offered by Euroscreen is that the annual licence fee is directly exchangeable for Euroscreen products, which in practice means these partners get around four AequoScreen™ cell lines a year for their annual fee or they could purchase specific membrane preparations or cell lines to that value. To date Euroscreen has announced nine corporate partnerships (which includes several non-pharma collaborations, eg CyBio) and other big pharma customers are believed to be on the verge of signing up. Thirdly, up until two years ago the main reading options for aequorin were limited to PMT-based readers with one to six injectors (eg Berthold MicroLumat or PerkinElmer MicroBeta Jet) which offered insufficient throughput for most HTS groups and the Molecular Devices FLIPR3 system whose success with aequorin is dependent on the signal intensities of the cell lines. However, the ability to detect aequorin today is markedly improved with the recent launches of three new dispense and image instrument platforms (CyBio CyBi™-Lumax, Hamamatsu FDSS and PerkinElmer LumiTrak™) able to read aequorin in 384 plates with high throughput. In addition, other instruments (eg Amersham Biosciences LEADseeker with integrated liquid handling) are in development. The comparative performance and features of the three available instruments is summarised in Table 2. As a word of caution the installed base of these instruments is a small number of units (especially for the

### Table 1

**Flash luminescence aequorin assays for calcium mobilisation (GPCR activation)**

#### BENEFITS

- Functional generic assay technology for the majority of GPCRs
- Simple combined assay protocol for agonists and antagonists
  - Harvest cells
  - Load cells with coelenterazine
  - Dispense cells on to plated compound and image
  - Dispense reference agonist on to cells and reimage
- Assays easier to automate, do not require cell washing or multi-step liquid handling
- Use of cell suspensions gives reduction in cell plating/maintenance costs
- Less compound interference (arising from auto-fluorescence and toxicity)
- Potentially less false positives than methods involving longer compound exposure
- Coelenterazine has little cellular toxicity and is not subject to efflux
- Stable loading for cells (up to 24h for some cell lines)
- Main reagent (coelenterazine) is very cheap (<$0.50/well)
- Intensity of light emission directly proportional to intracellular Ca\(^{2+}\)
- Large linear dynamic range with high calcium sensitivity in physiologic range
- No significant chelation of intracellular Ca\(^{2+}\)
- No binding to other divalent ions
- Targeted intracellular localisation in different cell types
- High signal-to-background, yields better quality data (higher Z' values)
- Greater potential for miniaturised formats (1536 plates)
- Higher sensitivity – less cells/well than fluorescent-based alternative assays

#### POSSIBLE LIMITATIONS

- Coloured compounds may reduce light emitted at 466nm (by inner filter effect)
- May need purchase of new dispense and image instruments (expensive)
- The need for higher throughput detection in 1536 plates
- In-house apoaequorin expression requires dedicated lab to support cell engineering
- Licence from Euroscreen required to transfect own cells with apoaequorin
### Table 2: Comparison of lum imagers for high throughput aequorin assays

<table>
<thead>
<tr>
<th>INSTRUMENT FEATURES</th>
<th>CYBIO CYBI™-LUMAX D</th>
<th>CYBIO CYBI™-LUMAX SD</th>
<th>HAMAMATSU FDSS 6000</th>
<th>PERKINELMER LUMITRAK™</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DISPENSING</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– dispensing mode</td>
<td>valve-less pump</td>
<td>valve-less pump</td>
<td>air-displacement</td>
<td>air-displacement</td>
</tr>
<tr>
<td></td>
<td>non-contact</td>
<td>non-contact</td>
<td>contact</td>
<td>contact</td>
</tr>
<tr>
<td>– number of channels</td>
<td>8 channels</td>
<td>8 channels</td>
<td>384 channels</td>
<td>384 channels</td>
</tr>
<tr>
<td>– number of heads</td>
<td>2 heads (1 optimised to cells)</td>
<td>2 heads (1 optimised to cells)</td>
<td>up to 3 heads</td>
<td>1 head</td>
</tr>
<tr>
<td>– tips</td>
<td>fixed nozzles</td>
<td>fixed nozzles</td>
<td>disposable tip or fixed needles</td>
<td>disposable tips</td>
</tr>
<tr>
<td>– volume range</td>
<td>0.5-50µL</td>
<td>0.5-50µL</td>
<td>0.5-10µL or 1-30µL</td>
<td>0.5-10µL or 0.5-30µL</td>
</tr>
<tr>
<td><strong>DETECTION</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– detector</td>
<td>image intensifier plus CCD, 2-D single photon counting sensor</td>
<td>image intensifier plus CCD, 2-D single photon counting sensor</td>
<td>image intensifier plus CCD, 2-D single photon counting sensor</td>
<td>back-thinned CCD, cooled to -100°C</td>
</tr>
<tr>
<td>– lens</td>
<td>Leica lens</td>
<td>CyBi™-Luminox lens</td>
<td>tapered fibre bundle</td>
<td>fibre-optic taper</td>
</tr>
<tr>
<td>– detection limit (sensitivity)</td>
<td>300fg/well or 1.5amol/well AquaLite®</td>
<td>30fg/well or 1.5amol/well AquaLite®</td>
<td>at least 30fg/well or 1.5amol/well AquaLite®</td>
<td>at least 30fg/well or 1.5amol/well AquaLite®</td>
</tr>
<tr>
<td>– dynamic range (for kinetic assay)</td>
<td>300fg – 100pg AquaLite® in photon-counting mode, 10pg – 10ng in analog mode</td>
<td>30fg – 10pg AquaLite® in photon-counting mode, 1pg – 1ng in analog mode</td>
<td>data not available</td>
<td>between 300fg - 1ng/well AquaLite® (0.44s integration time)</td>
</tr>
<tr>
<td>– linearity</td>
<td>up to 50ng/well or 25fmol/well AquaLite®</td>
<td>up to 5ng/well or 2.5fmol/well AquaLite®</td>
<td>data not available</td>
<td>up to 1ng/well or 0.5fmol/well AquaLite®</td>
</tr>
<tr>
<td>– acquisition (frame) rate</td>
<td>~25 images/sec</td>
<td>~25 images/sec</td>
<td>~30 images/sec</td>
<td>1 image/0.6sec</td>
</tr>
<tr>
<td><strong>OTHER</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– light sources</td>
<td>✗</td>
<td>✗</td>
<td>✓ (optional lamp)</td>
<td>✗</td>
</tr>
<tr>
<td>– fluorescence mode</td>
<td>✗</td>
<td>✗</td>
<td>✓ (optional separate detector)</td>
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<tr>
<td>– filtered emission</td>
<td>✗</td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>throughput – plates/hour (single agonist injection)</td>
<td>20x384 or 10x1536</td>
<td>10x384 or 5x1536</td>
<td>25x384</td>
<td>1536 in development</td>
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<tr>
<td>Approx. cost (from)</td>
<td>$195,000</td>
<td>$245,000</td>
<td>$390,000</td>
<td>$450,000</td>
</tr>
</tbody>
</table>
most recently launched LumiTrak™). So in some respects the robustness of these platforms in routine HTS is not fully proven.

**New flash solutions open way to higher throughput**

The new generation of flash luminescence detectors capable of higher throughput analysis, utilise different optical and imaging solutions. In the case of LumiTrak™ a single fibre-optic taper is coupled directly to a cooled (-100°C) back-thinned CCD. This CCD has high quantum efficiency in the blue and red emission spectra with an ability to acquire whole plate images in kinetic mode or integrate weak signals. The fibre-optic taper enables ‘contact imaging’ – a patented means of highly efficient light gathering without parallax, no reflection, minimal cross-talk or the focusing requirements of a normal lens. The other systems (ie CyBi™-Lumax and FDSS) both use a 2-D image intensifier with transfer optics to an uncooled CCD that enables single photon counting. The input window of the intensifier is a photocathode which converts photons to electrons just like a PMT. The difference is that the intensifier also gives area information. The location of the photon event is transferred to the output of the intensifier so that the readout camera can not only measure the intensity but record the geography as well. The specialty of this technology is that single photons are amplified with an extremely low background, keeping the two-dimensional positional information of the detected photons, thereby intensifying the image. Interestingly, both instruments (CyBi™-Lumax and FDSS) use Hamamatsu image intensifiers, so performance differences relate mainly to the optical elements, associated hardware (dispensing system) and the software. Both the CyBi™-Lumax SD and CyBi™-Lumax D use lenses between the intensifier and the plate, while the FDSS couples the input of the intensifier to the bottom of the plate using a tapered fibre bundle. The CyBi™-Lumax SD uses a proprietary lens with a high optical aperture and reduced shading (CyBi™-Luminox) and images only part of the microplate at a time. Thereby, its collection efficiency is substantially
higher than in the case of imaging the microplate as a whole. Both the CyBi™-Lumax and FDSS in photon counting mode apply a threshold to the data to discriminate a *bona fide* photon event from camera and cosmic noise. This is done with a time-resolution of 40 milliseconds. The photons are then integrated over the recording time making this a nearly noise-free technique. Alternatively, for high signals the CyBi™-Lumax software supports the accumulation of raw analog data in analog mode. This mode allows detection of high signals that would cause saturation in photon counting mode thereby increasing the overall dynamic range of the CyBi™-Lumax system. In contrast, a cooled CCD has a wider dynamic range, between four and five orders of magnitude. Shading can be an issue for intensified imagers. CyBio offers shading correction by software and has developed tools for the easy determination and correction of the shading effect. Both cooled CCD cameras and photon counting (image intensifier) cameras require integration. The difference is where they integrate. A cooled CCD integrates images on the CCD chip before read-out. Thus the cooled CCD requires longer exposure times at low light levels (ie slow frame rate). On the other hand, the photon counting camera integrates the images on computer memory after read-out. The frames are read out quickly (ie fast frame rate), but need a certain integration time after read-out. So comparing frame rate can be misleading, a more useful measure is the potential throughput that can be achieved reading an aequorin assay (eg for a single agonist injection) in a 384 plate (see Table 2) as this takes into account differences in the liquid handling set-up. All systems described are capable of reading at least 20x384 plates/hour or approximately 50,000 data points per working day if you include set-up time etc, some have significantly higher throughput, such as LumiTrak™.

**How important is instrument sensitivity?**

All of these new generation flash imagers are sufficiently sensitive to detect around 30fg/well or 1.5 amol/well AquaLite®, under optimal conditions. AquaLite® (Molecular Probes) is a useful test substance to optimise luminescence detection and is the registered tradename for purified, cell-free aequorin that is produced by purifying apoaequorin from recombinant *E. coli* bacteria followed by reconstitution of the complex with pure coelenterazine. The actual sensitivity delivered by the detection systems is a tradeoff between the throughput required and the number of cells/well used, eg the CyBi™-Lumax D is optimised for maximum throughput, while the CyBi™-Lumax SD is optimised for maximum sensitivity, while PerkinElmer has attempted to optimise both on LumiTrak™. In practice, sensitivity for aequorin cell lines may vary as intensity is dependent on receptor and apoaequorin transfection efficiencies, in addition to cell viability. However, instrument sensitivity is not now per-
ceived as limiting, particularly as Euroscreen has recently developed new aequorin cell lines with much improved emission brightness. The difference is such that previously it was generally recognised that FLIPR3 had poor sensitivity for aequorin assays, but assays with the new aequorin clones have now been demonstrated on FLIPR3. The luminescence change with AquaLite® at 1ng/well stimulated by 10µM CaCl₂ compares very closely with the flash luminescence signal with aequorin assays run on FLIPR3. The signal originated by the new ADM (Adrenomedullin receptor) AequoScreen™ cell line is within the dynamic range of detection for FLIPR3 and suggests that the FLIPR3 can be effectively used to detect flash luminescence signal from selected AequoScreen™ cell lines.

Although not the focus of this article, we should not overlook the fact that the detection sensitivity of these new imagers is also adequate for chemiluminescent applications involving weak isotopes or using Amersham’s SPA and LEADSeeker beads and PerkinElmer’s clear bottomed FlashPlate and new FlashBlue and FlashRed™ GPCR scintillating beads. The instruments are also suitable for a broad range of other flash luminescence assays, eg those using luciferase aimed at measuring cell number or viability via ATP content or measuring reporter gene expression. Flexibility to read alternative fluorescent-based dispense and image technologies in the same instrument capable of flash luminescence is a feature unique to the FDSS and the FLIPR3.

**Standalone operation versus robotic integration**

One of the key benefits of aequorin assays is their protocol simplicity relative to fluorescent-based alternatives and the reduced need for complex automation. The necessity to integrate flash luminescence imagers into a larger robotic system to provide automated processing is now much reduced, as it is possible to process a reasonable batch of plates (up to 200 plates) on these turnkey workstations. All of the instruments discussed in Table 2 have plate stacking, cell suspension and refillable reagent capability so that walk-away automation can be achieved, although the screening of antagonists (which involves a second liquid addition of a reference agonist) will be simpler and potentially faster on those systems that have multiple dispense heads (CyBi™-Lumax and FDSS) and specially designed nozzles for cell dispensing (CyBi™-Lumax). On the other hand, LumiTrak™ offers automated tip wash and multiple platform positions to accommodate compound, antagonist and assay plates, where agonist and antagonist incubations are timed and automated. The co-marketing relationship between CyBio and Euroscreen is of interest in that CyBio can now provide aequorin assay biology and assay support fitting to the CyBi™-Lumax system in a package with protocols optimised to specific AequoScreen™ cell lines, minimising assay development time for the end-user. It is too early to tell how the CyBi™-Lumax and LumiTrak™ systems will be deployed by groups intending to run large diversity aequorin screens. Interestingly, a significant number of FDSS systems in Japan have been integrated into robotic systems. For those chemi-luminescent applications
involving weak isotopes or SPA, the benefits of integrated liquid handling are less apparent and the majority of pharma customers would probably prefer a small footprint standalone detector which they could integrate into their existing robotic line.

Prospects for 1536 assays
The non-contact dispense mode of the CyBi™-Lumax Drop dispenser clearly differentiates it from the other offerings, and is particularly advantageous for 1536 plates and lower volume assays (≤5µL). Non-contact operation makes tip washing between assay plates unnecessary and automated tip loading and disposal are avoided with two dispense heads. Together these activities occupy a large percentage of time in a typical aequorin assay cycle. Although most systems discussed in Table 2 are ‘compatible’ with 1536 plates and can image entire 1536 plates, the four-fold increase in throughput that might be expected to result from 1536 relative to 384 currently is not realised. This is because the simultaneous dispensing of liquid (cells or agonist) to all 1536 wells in a highly parallel mode at the reading position cannot be achieved with a 384 channel dispense air-displacement head if tip washing is required between dispenses. The parallel processing capability of LumiTrak™ allows tip washing while the instrument is reading, which improves 1536 capability. CyBio is working on a further development of the CyBi™-Lumax D, that will increase its throughput for 384 and 1536 by factor two (i.e. to 40x384 and 20x1536 per hour). If CyBio was to combine CyBi-Lumax D luminescence detection with its integrated CyBi™NanoJet injection technology, a throughput of 30x1536 plates per hour might be possible. A 384-channel, ideally non-contact, dispenser in which the dispense-head was rapidly moved in four steps above a continuously imaged fixed 1536 plate might further reduce assay cycle time to under one minute. Of the alternative dispensing technologies available today, only 1536 pin tools could provide immediate access to simultaneous 1536 assays, but pin tools have limitations in terms of their dispensing accuracy, the ability to promote rapid liquid transfer and mixing and they require contact between pin and the assay plate or medium in the well. The suitability of pin tools to dispense cells in the 0.5 to 10µL range is also debatable (pin tools delivery is more suited to nL volumes). There are no known 1536 air-displacement (contact) dispense heads (with fixed needle/cannula or disposable tips) and highly parallel non-contact systems with this capability have yet
to be commercialised. In principle, a 1536 head based on GSI’s Hummingbird™ technology might be manufactured, although the packing density would preclude the current 384 head design which is based on removable capillaries housed within plastic sheaths. However, since the head would primarily be used to dispense common aqueous-based reagent (cells or agonist) it would not need to enter deep well blocks (one of the benefits derived from the extended capillary sheath) and washing would be less of an issue relative to DMSO-based compound reformatting. The relatively compact nature of the Hummingbird™ head and the associated pressure actuation unit would make it well suited for integration into imaging devices. Some might argue that high density aequorin assays need a totally different liquid handling approach. For example, Abbott Laboratories has demonstrated aequorin assays using its mARCS platform based on adding cells to an agarose gel and combining this gel with compounds arrayed in a free format on a sheet. However, Abbott relied upon the delayed response of coelenterazine 1 to provide them a wider flash luminescent imaging window. Perhaps the BD Falcon 1536-Virtual Well Plate could address the fluid handling problem of initiating 1536 reactions simultaneously. The Virtual Well Plate consists of matched lid and base halves, each having a framed 1536-well array of hydrophilic ‘well spots’ on a hydrophobically masked glass slide. By distributing compounds to one half of the sandwich (eg base) and aequorin cells to the other (eg lid), it should be possible to do tests for agonists, although separating the plate pair to bring in a reference agonist (eg on a new lid) to test for antagonists may be problematic. Until an instrument manufacturer is convinced about the need for ultra high throughput, simultaneous 1536 flash luminescence assays look set to be rate-limited within existing instruments.

**Assay services based on aequorin**

Euroscreen offers screening services particularly suited to those customers who only want to screen a relatively small number of compounds but lack the capability or capacity to perform the task in-house. Several thousands of compounds can be managed with a turnaround time of only four weeks. Euroscreen performs functional HTS with its proprietary AequoScreen™ platform on a fee-for-service basis (prices start at around €7 per data point for a sequential agonist and antagonist screen, but are subject to volume discounts) or as part of a drug discovery collaboration. Evotec OAI has licensed Euroscreen’s GPCR reagents, including cell lines, membrane preparations, as well as functional analyses using AequoScreen™ technology, and may develop aequorin drug screening products and contract services to the biopharmaceutical industry. More recently, CyBio extended its co-marketing agreement with Euroscreen into a co-operation agreement enabling CyBio Screening GmbH to claim to be a ‘one-stop-shop’ for screening services against GPCR receptors using AequoScreen™ cell lines. Assays are validated and automated in 384 well plates using CyBi-Screen robots equipped with CyBi™ Lumax detectors and CyBio has adequate compound logistics to accommodate the screening of large third-party libraries. CyBio also makes use of its latest software developments to accelerate the screening adaptation process and generates high quality aequorin data using its CyBi™, SIENA software for the elimination of systematic errors. Hamamatsu’s close working relationship with Euroscreen, which dates back nearly four years when they both started developing an aequorin capable instrument, means FDSS customers also benefit from excellent AequoScreen™ support. In addition, Molecular Devices is providing customers with continuing applications support to optimise detection of some bright aequorin assays on FLIPR3.

**Other photoproteins**

Clearly photoproteins (like aequorin) represent a very important tool in the modern drug discovery process. In general, photon emitting reactions are calcium dependent. Therefore, photoproteins can be applied to the detection of calcium release triggered by several receptors and ion channels. The typical time to peak signal is within five seconds, which favours the detection of real target molecular interactions, versus potentially misleading compound interactions on transcription and translation related proteins, as is the case in standard reporter gene assays. Axxam has generated several new and improved photoproteins in order to improve calcium sensitivity and quantum release. One of them is called Photina™ and it shows an increased quantum release, compared to other photoproteins. This characteristic also allows for detection of a robust calcium signal in very few cells which may facilitate the transition to 1536. The kinetic measurement of photon release by Photina™ either under low or high throughput screening conditions has been demonstrated using both the CyBi-Lumax™ and FLIPR3 instruments.
Summary
The benefits of the aequorin approach to functional GPCR activation assays are undisputed. The advent of a more realistic licensing strategy by Euroscreen for AequoScreen™ technology, the recent emergence of several alternative detection platforms optimised for higher throughput flash luminescence analysis, the availability of new aequorin screening services and the development of new photoproteins suggest there has never been a better time to consider or revisit flash luminescence technology for functional calcium release assays. The potential for increased use of photoproteins in screening looks bright.

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Dr John Comley is Managing Director of an independent market research consultancy (www.htstec.com) whose focus is on assisting clients delivering novel enabling platform technologies (liquid handling, detection instrumentation and assay methodologies) to the HTS environment. Previously as Manager of HTS Technologies at PerkinElmer, Turku, he was responsible for the development of SmartStation. Dr Comley has more than 20 years' experience in drug discovery and was formerly Principal Scientist at GlaxoWellcome, UK where he pioneered assay miniaturisation. Dr Comley undertook post-doctoral work at the Universities of Vermont and Liverpool and has a PhD in Parasite Chemotherapy from Imperial College, London University.