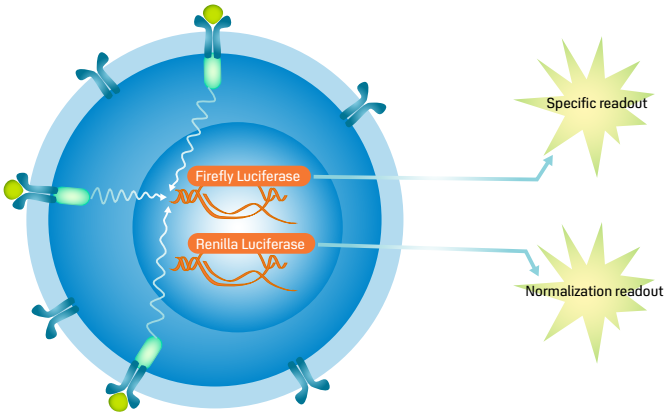
iLite® Technology

CELL-BASED REPORTER GENE ASSAYS

A versatile tool for **the whole drug development process**

***The iLite* technology provides a seamless solution for applications extending across the whole drug development process, as well as for monitoring of biological drugs. The technology can be applied to many different drug targets and allows an easy, rapid and accurate test format for measurement and quantification of drug potency and immunogenicity. By combining unique features such as a normalization readout and chimeric transcription factors with a highly flexible product format, the *iLite* technology helps you make the most of your bioassay.**

The *iLite* technology is based on a dual reporter gene system. When a ligand binds to its receptor, its specific intracellular signaling pathway is activated, triggering the transcription of a specific reporter gene construct coding for Luciferase. The amount of luciferase and thereby the activity of the ligand can then be measured as light emission using a luminometer. The *iLite* cells also contain a second reporter gene which is under the control of a constitutive promoter, and is thus expressed continuously. This secondary readout can be used for normalization purposes, as it will correlate to the number of viable cells.



The cell lines are engineered using target specific reporter gene constructs designed to not respond to other factors that signal through the specific pathway. This way a specific and precise assay can be engineered. The readout is light emission as measured by a standard luminometer.

ASSAY READY CELL FORMAT

The Assay Ready Cell format removes the need for cell culture and continuous maintenance of cells. The cells are simply thawed and diluted before use in the assay. Besides significant reductions in labor and assay times, the Assay Ready Cell format also gives superior reproducibility, since all cells are cryopreserved at the same passage number.

NORMALIZATION GENE

Normalization can be performed using the second reporter gene, and will compensate for differences in cell number, a major benefit when encountering serum matrix effects. Normalization can also be used if the luciferase is sensitive to your compound, as can occur during high-throughput screening procedures.

HIGH SENSITIVITY & PATHWAY SPECIFICITY

The sensitivity of *iLite* cells is enhanced through up-regulation of key components, such as the receptor and certain signaling pathway proteins. The high specificity is obtained by using chimeric transcription factors and synthetic promoters, rendering endogenous transcription factors unable to trigger expression of the reporter gene and thus eliminating cross talk.

A seamless solution for accelerating drug development

A significant benefit of the *iLite* technology is that the *iLite* cell-based reporter gene assays can be used throughout the whole drug development continuum. As functional, cell-based assays, they can deliver accurate and biologically relevant results all the way from high throughput screening, through CMC lot release testing, to determination of immunogenicity.

Target discovery & validation	HTS compound screening	Preclinical evaluation of efficacy, safety PK	Manufacturing process development quality control	Clinical development phase II/III	Approval	Post market surveillance	Innovator & biosimilar approval
		iLite® Potency assay		***iLite***® Circulating active drug levels and NAb quantification			***iLite***® Direct comparison of innovator & biosimilar in one single assay

iLite® Screening for new drug candidates

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FEATURES	BENEFITS
• *iLite*® reporter gene cells are delivered as **Assay Ready Cells** and give results within a day	**Fast and convenient use**
• **Screening, potency** and **neutralizing** antibody assays can be perfomred using a single reporter gene cell line	**Multiple assays using a single reporter gene cell line**
• The mechanism of action is accurately reflected since **signaling pathways are maintained**	**Biologically relevant results**
• **Direct comparisons** between biosimilars and originator/innovator drugs and **unrivalled specificity** to distinguish between structurally related drugs - in one single *iLite*® assay • A **single assay** for structurally diverse drugs in the same class (such as TNF-alpha antagonists)	**Standardization and economy of costs**
• **Normalization gene,** expressing a second Luciferase, allows normalization for matrix effects as well as cell numbers	**Normalization of results**

FDA recommends bioassays for potency and immunogenicity assessments during development of biologicals:

"Ideally, the potency assay will represent the product's mechanism of action (i.e., relevant therapeutic activity or intended biological effect)" (5).

"Generally FDA considers that bioassays are more reflective (than competitive ligand-binding assays) of the in vivo situation and are recommended" (6).

"FDA recommends that neutralization assays use a cell-based bioassay format depending on the therapeutic protein product's mechanism of action because, frequently, cell-based bioassays more closely reflect the in vivo situation and therefore provide more relevant information than ligand-binding assays." (7).

Intellectual Property

References

1. Lallemand C, Kavrochorianou N, Steenholdt C, et al. Reporter gene assay for the quantification of the activity and neutralizing antibody response to TNF alpha antagonists. *J Immunol Methods. 2011 Oct 28;373(1-2):229-39.*
2. Tovey MG, Lallemand C. A Novel cell-based assay for the quantification of neutralizing antibodies to biopharmaceuticals. In: Michael G Tovey, ed. *Detection and Quantification of antibodies to biopharmaceuticals: Practical and Applied Considerations.* New York; John Wiley & Sons Inc; 2011: 283-299.
3. Tovey MG, Lallemand C. Improved analytical methods for the detection and quantification of neutralizing antibodies to biopharmaceuticals. *Bioanalysis. 2012 Sep;4 17:2179-90.*
4. Pavlov IY, Carper J, Lázár-Molnár E, Delgado JC. Clinical laboratory application of a reporter-gene assay formeasurement of functional wactivity and neutralizing antibody response to infliximab. *Clin Chim Acta. 2016 Jan 30;453:147-53.*
5. Guidance for Industry: Potency for cellular and gene therapy products, issued by FDA, Jan 2011.
6. Guidance for Industry: Assay Development for Immunogenicity Testing of Therapeutic Proteins, issued by FDA, Dec 2009.
7. Guidance for Industry: Assay Development and Validation for Immunogenicity Testing of Therapeutic Protein Products, Draft Guidance, Apr 2016.

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