

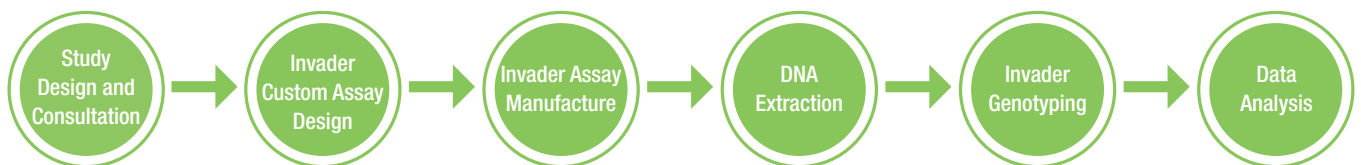


TEPNEI
Pharma Services

Invader® & InvaderPlus® Service

Tepnel Pharma Services offers a fully customisable service utilising Invader and InvaderPlus chemistries for biomarker discovery, assay development, assay validation and companion diagnostic development in support of pre-clinical, clinical and personalised medicine studies.

The Invader chemistry platform is a proprietary, cost effective isothermal, DNA-probe based system utilised in a wide range of applications. Invader chemistry is currently used in multiple FDA approved and CE marked products and is used extensively by laboratories worldwide for their clinical diagnostic, research and high throughput genotyping and gene expression needs.



Invader and InvaderPlus assays are suitable for a wide range of applications including genotyping, copy number variation, gene expression and detection of InDels. Invader and InvaderPlus chemistries are:

- Cost effective across a wide range of target and sample numbers
- Scalable and automatable
- Proven track record for use in FDA approved companion diagnostic tests
- Works with a wide range of tissue types including FFPE
- High assay conversion rate
- Low incidence of false positives

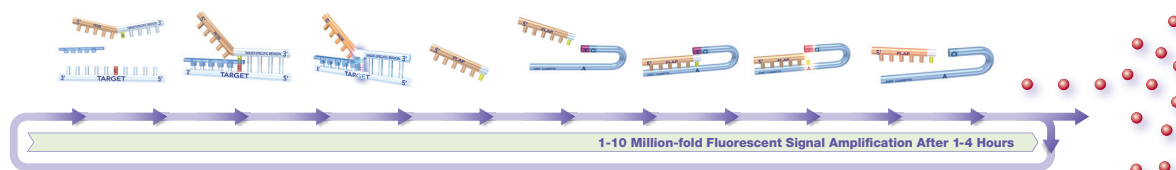
Invader Chemistry

Simple, scalable and accurate

Tepnel Pharma Services offers a high-throughput, cost-effective service using the Invader and InvaderPlus chemistries:

- A proprietary, patented technology
- Detects specific nucleic acid sequences (template can be DNA, RNA or microRNA)
- Invader is a direct isothermal genomic assay
- InvaderPlus combines sensitivity of PCR and specificity of Invader
- Structure specific recognition and cleavage by Cleavase® family of enzymes
- Fluorescence detection

Invader® Chemistry: Simple, Scalable, Accurate



Primary Reaction

In the first reaction, two oligonucleotides, a probe and an Invader oligo, anneal to a specific DNA target sequence to generate a one-base overlapping structure if the desired sequence is present. Each time an intact probe molecule binds to the specific target in the presence of the Invader oligo, the overlapping substrate is formed and cleavage occurs. The number of flaps released is relative to the amount of target in the sample, allowing for quantitative detection of genes, chromosomes or infectious agents.

Final Results

Each released 5' flap from the primary reaction continually binds and releases from the FRET cassettes, enabling the secondary reaction to further amplify the target-specific signal. The two simultaneous reactions typically produce a 1-10 million-fold signal amplification during a 1-4 hour reaction.

The use of discriminatory primary probes (wild-type and mutant), and two corresponding FRET cassettes, each with a distinct fluorophore, produces target-specific signals that allow for distinguishing between wild-type, mutant and heterozygous-target sequences.

Secondary, Simultaneous Reaction

Cleaved flaps from the primary Invader reaction combine with a fluorescence resonance energy transfer (FRET) probe in a secondary, simultaneous overlapping cleavage reaction, generating a fluorescent signal. The combination of two different flap sequences, FRET oligos, and fluorophores allows for single-well biplex reactions to occur.

HOLOGIC®

Europe

Appleton Place
Appleton Parkway
Livingston, West Lothian
EH54 7EZ, UK
T: +44 (0)1506 424270
E: pharma@hologic.com

Heron House
Oaks Business Park
Crewe Road, Wythenshawe
Manchester, M23 9HZ, UK
T: +44 (0)161 946 2200
E: pharma@hologic.com

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