Vipergen
The inventor of the YoctoReactor®

# High fidelity drug discovery - Get an early lead

**Vipergen introduces the YoctoReactor® (yR) and Binder Trap Enrichment® (BTE) technologies, 2nd generation DNA-encoded chemical library technologies designed to efficiently deliver the highest fidelity primary screening results in the industry.**

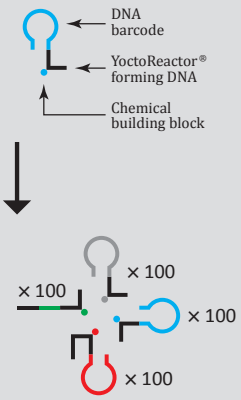
- Multi-million member small molecule libraries screened in a single tube
- Libraries optimized for oral bioavailability
- Generally applicable across disease areas and soluble drug target classes
- Applicable to difficult targets (including PPI)
- Instant ligand-target half-life, SAR and specificity
- Hit series identified in a few weeks, fully validated within 3-6 months

Fidelity defines our drug discovery technologies and enables the generation of unambiguous primary screening data in a simple, single screen. Fidelity between the DNA-code and the synthesized small molecule is ensured by the precise 3D design of yR libraries featuring intrinsic error prevention. As a homogeneous assay, BTE delivers high fidelity by avoiding surface artifacts and the complexity of matrix binding. Fidelity, inherent in these complementary technologies, coalesce, to efficiently generate hits for even challenging protein targets while integrating kinetic and thermodynamic criteria for comprehensive SAR analysis.

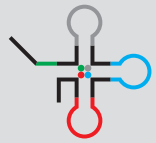
**Partner's protein target** → **Protein target(s) labeled with DNA** → **Binder Trap Enrichment®** → **Hit identification and evaluation** → **Synthesis and testing of hits (DNA-free compounds)** → **Bioactive hits, instant ligand -target half-life, SAR and selectivity** → **Improved starting point for lead optimization**

## YoctoReactor® library synthesis

### Ready-for-use



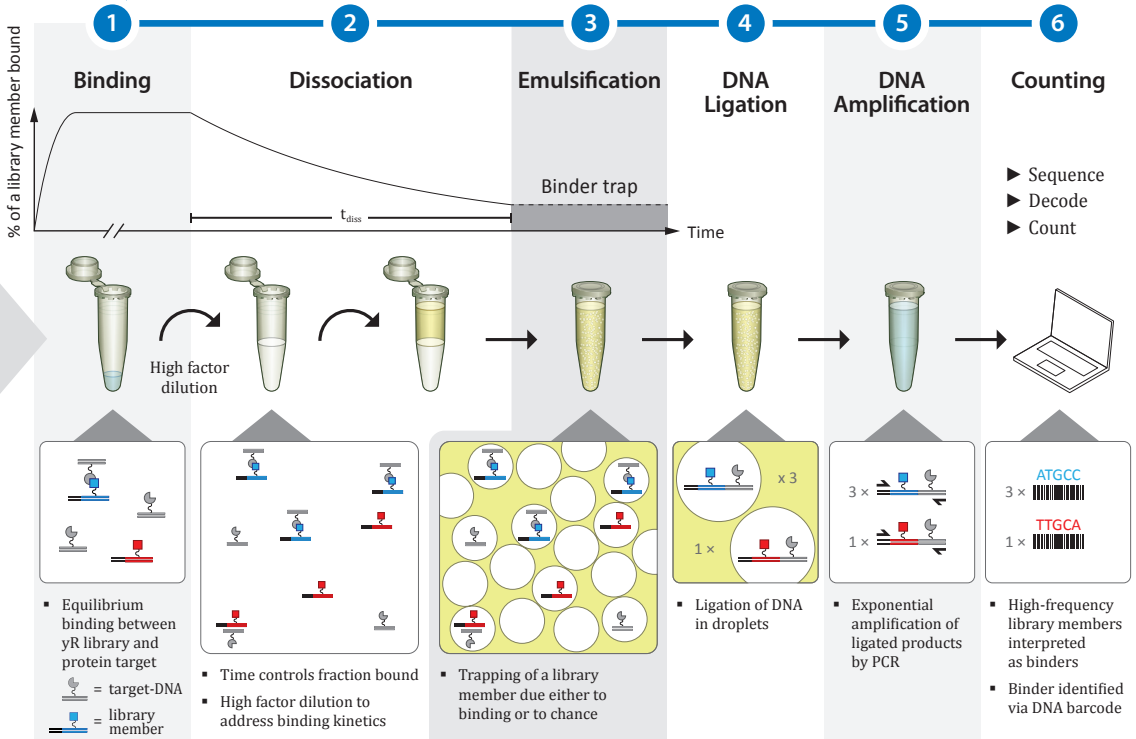

- Self-assembly
- Chemical reaction
- Purification
- DNA ligation
- Linker cleavage
- Purification



Diversity = $1 \times 10^8$

- Primer extension

## Binder Trap Enrichment®




- Equilibrium binding between yR library and protein target
  = target-DNA
  = library member
- Time controls fraction bound
- High factor dilution to address binding kinetics
- Trapping of a library member due either to binding or to chance
- Ligation of DNA in droplets
- Exponential amplification of ligated products by PCR
- High-frequency library members interpreted as binders
- Binder identified via DNA barcode

### Key features of YoctoReactor®

- 3D proximity driven chemistry
- High fidelity between DNA code and small molecules
- No truncated or unreacted products due to purification steps
- Single tube process

### Key features of Binder Trap Enrichment®

- Mimics the dynamic binding conditions taking place in the human body
- Solution based (homogenous assay)
- Low amounts of target protein required (µg)
- Taps into high capacity DNA sequencing technology
- High fidelity process (low false positive rate)

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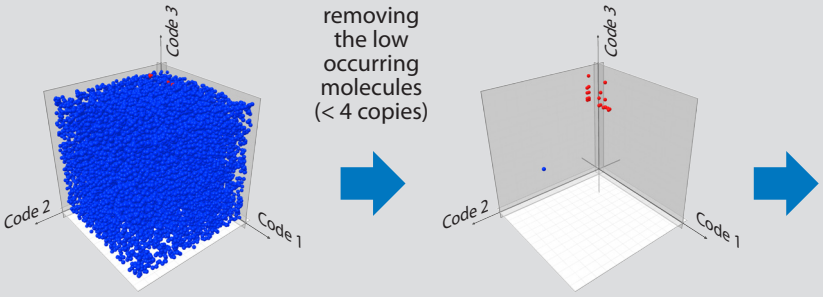
# Case Study: Map Kinase 14 (MAPK14)

## Results after 1 round BTE with yR library

- Target: Map Kinase 14 (MAPK14)
- Library: Lib020 (2.4 million compounds)
- Selection: BTE (one round)
- Output assay: DNA sequencing
- After BTE: positives signals emerge from the DNA sequencing data set by removing the molecules which are observed less frequently (< 4 copies) revealing a cluster of structurally related compounds
- The low false positive rate attributed to high fidelity yR library in combination with stringent BTE methodology
- Straightforward identification of hits and hit families

## Description of yR Library 20 (Lib020)

- Size: 2.4 million compounds (140 × 120 × 140 BBs)
- Oral bioavailability: 90% in compliance with RO5
- Diversity oriented synthesis (combinatorial)
  1. BBs cover a diverse range of pharmacophore motifs
  2. 3 different chemistries in two steps:
     a) Acetylation
     b) Reductive amination
     c) Urea formation
  3. Linear and branched compounds
  4. >10 types of traces




20 545 reads

23 structural related hits (red)
1 unrelated structure (blue)

3D scatter plot – a sphere represents a compound identified by DNA sequencing after a single round of BTE

## Assay (DNA-free compounds)

- 12/12 tested hits bind ($K_d$ 80 nM–10 µM)
- 12/12 tested hits inhibit ($IC_{50}$ 130 nM–597 µM)

- ► Very low false positive rate
- ► iSAR
- ► >1000 fold enrichment

## Immediate Benefits of yR/BTE

- ► Identify hits and hit families delivering SAR for instant evaluation of functional groups critical to the binding interaction
- ► Address selectivity instantly by parallel selections on families of targets
- ► Appropriate across therapeutic areas for soluble proteins (no structural information required)

## Why?

- ► Generate superior chemical starting points and provide medicinal chemists with a superior vantage point for lead optimization
- ► Complements and supports acceleration of Hit-to-Lead optimization efforts

## Collaborating with Vipergen

Vipergen is actively seeking collaborations and partnerships with leading pharmaceutical and biotech-nology companies to leverage the unique yR and BTE technologies and Vipergen's drug discovery expertise towards the efficient identification of validated hits for therapeutically important and difficult targets.

## About us

- ► The YoctoReactor® and Binder Trap Enrichment® technology platforms are exclusively owned by Vipergen and are secured by strong patent positions
- ► Founded in 2005 and incorporated in Copenhagen, Denmark
- ► Privately owned by Dr. Nils Hansen, Gunnar Kjems and Eigil Bjerl Nielsen
- ► Currently 9 employees, all PhD

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