

Controlled gene expression in the liver

Design of constitutive, inducible and repressible promoters for use in gene medicine

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the leader in gene control

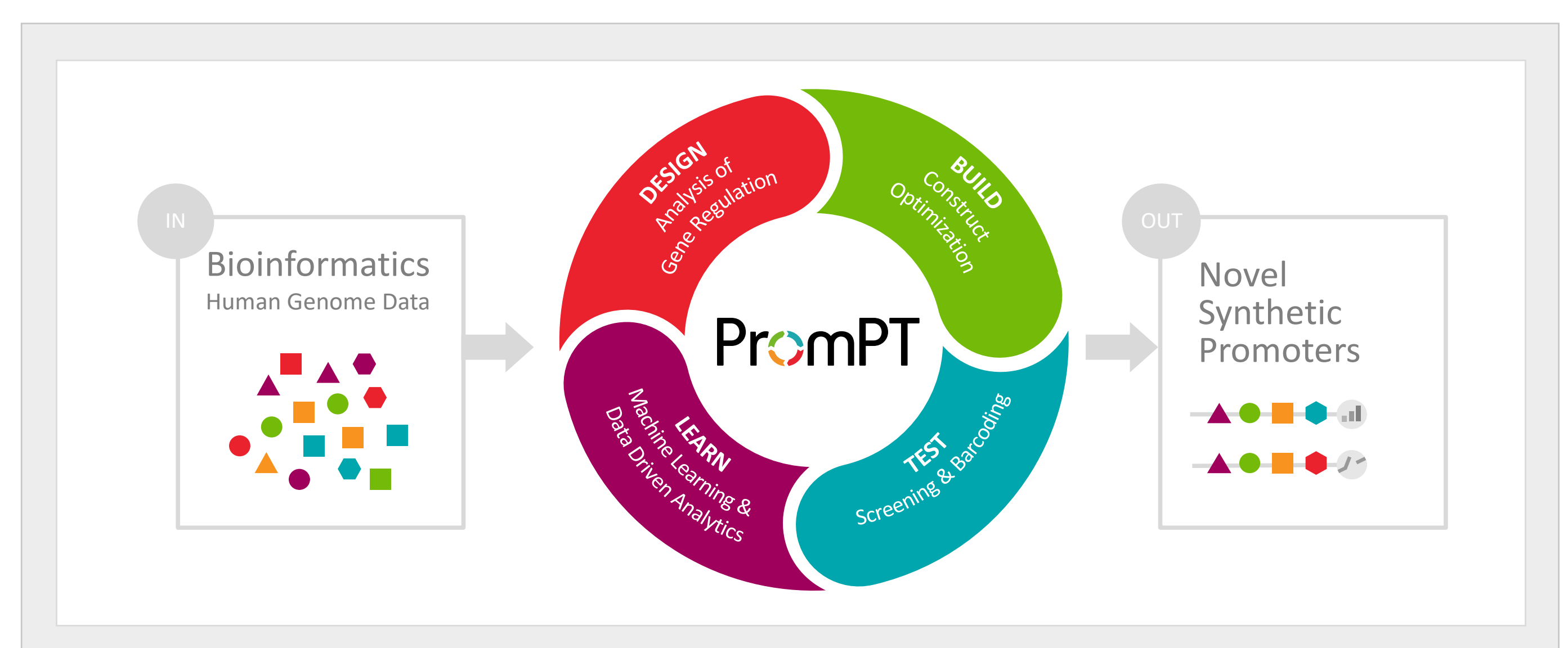
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Developing tissue selective promoters

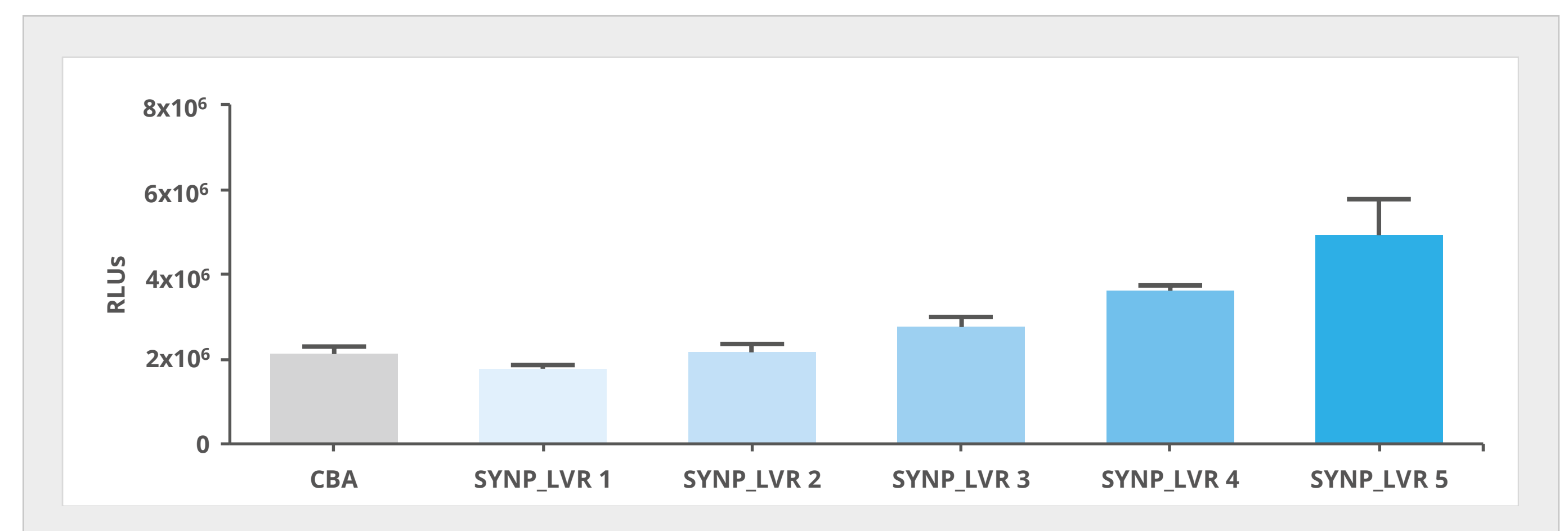
Promoter precision technology - PromPT[®]

- Promoter design platform
 - Integrates large-scale functional genomic datasets
 - Processed using machine learning algorithms
 - Identify functional gene regulatory elements
 - Elements are then ranked
 - Used to generate synthetic promoters
 - Required strength, size and specificity
- Constitutive, Inducible, Repressible, Self-regulatory
 - Gene regulation tailored to need
 - Gene expression cassette optimisation
 - ITR's
 - UTR's
 - Introns
 - Insert



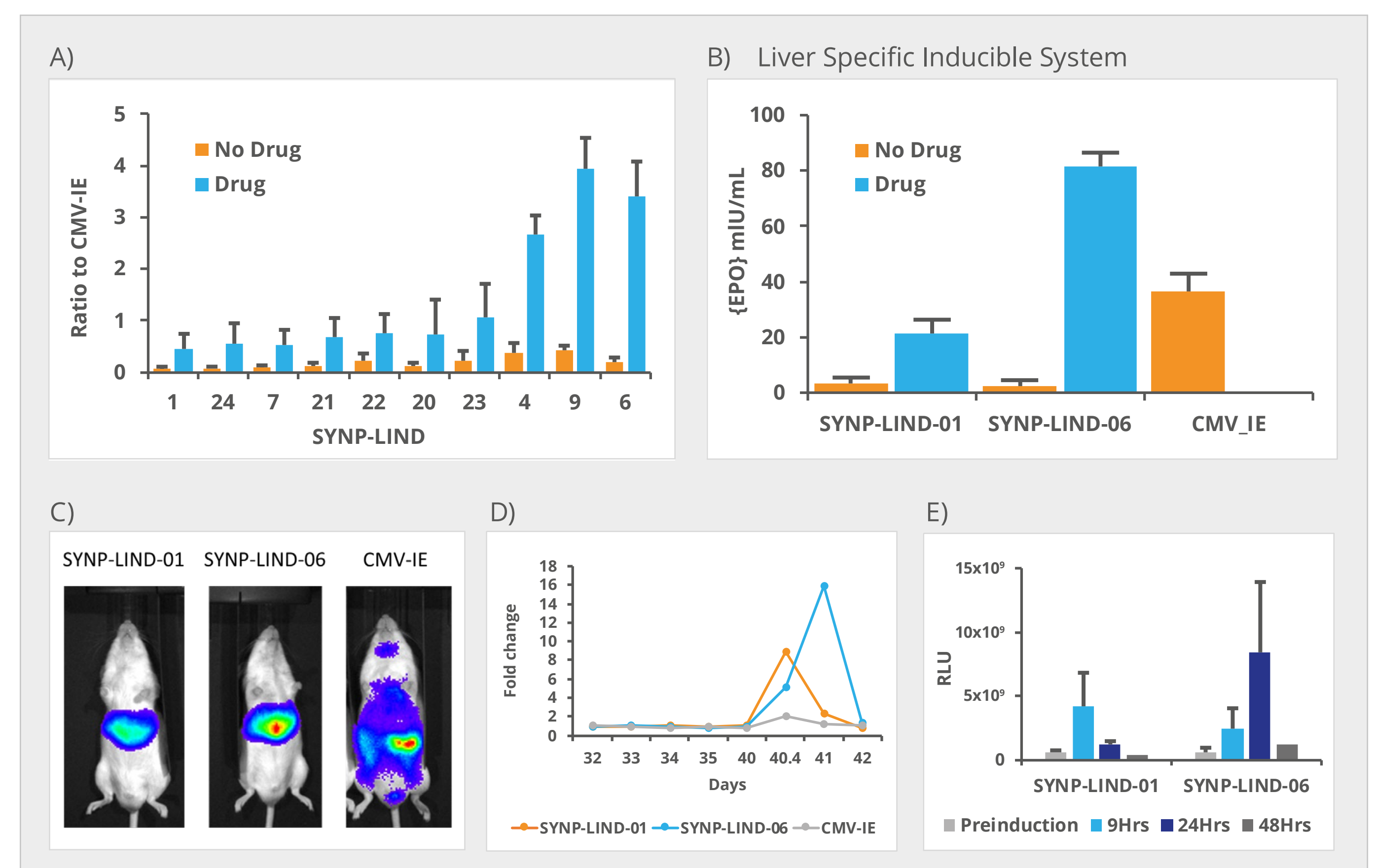
Design of small and strong liver-specific constitutive promoters

- PromPT[™] was used to identify liver-specific CREs
- These CREs were used to design small highly active liver-specific promoters
- Promoters were tested in Huh7 cell line
- Specificity tested in non-liver cell lines
- The promoters shown here are a subset of a range of promoter strengths



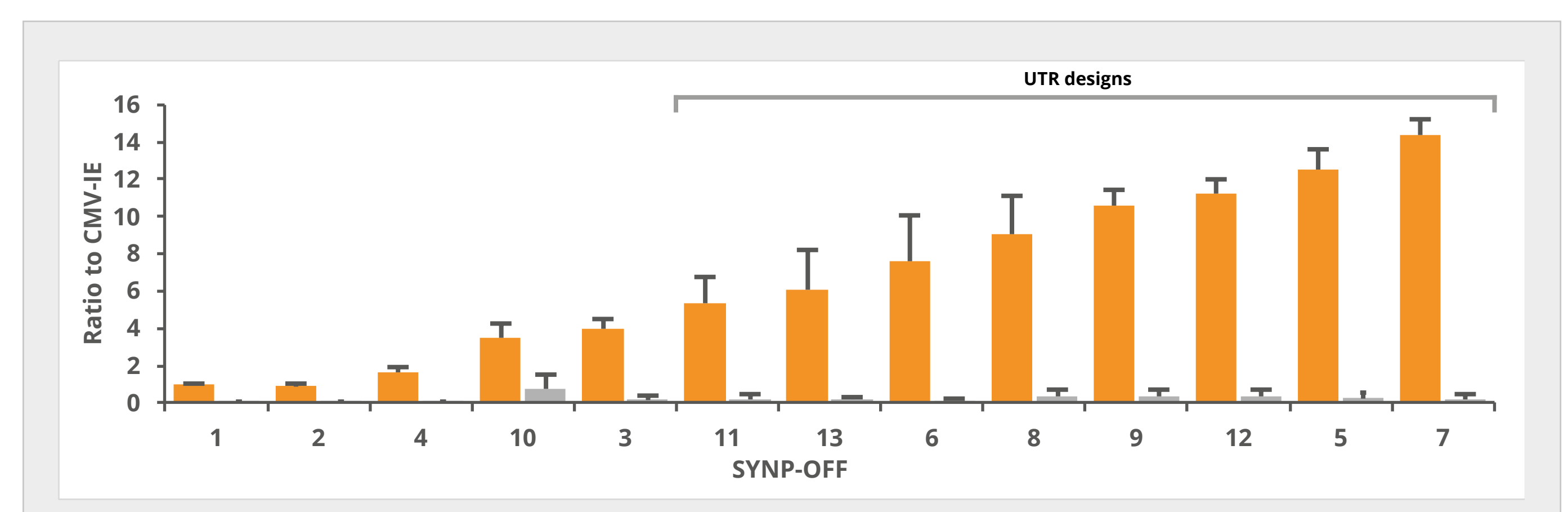
Development of novel liver-specific inducible promoters

- PromPT[®] can also be used to design small molecule inducible promoters (A)
 - Inducer is GRAS/FDA approved
 - Engineered promoters with wide a dynamic range
- Robust expression regardless of transgene (B)
- Using our technology tissue specificity can be incorporated (C)
- Induction can be tailored (D and E)
 - Configuration of promoter determines magnitude and time of response
- These one component systems offer many advantageous over other systems
 - Small, tissue specific, configurable



Creation of novel liver-specific repressible promoters

- Using PromPT[®] we identified liver-specific repressible CREs
 - Reactive to GRAS status chemical
- Designed promoters for strength, repressibility and specificity
 - Strong highly repressible activity
- Modified the expression cassette by incorporating UTRs identified via PromPT[®]
 - Demonstrated an expression range of 0 - 15 fold CMV-IE from 1 promoter design



The Synpromics PromPT[®] platform enables the identification and the design of elements to enhance and/or control gene expression to the appropriate level for therapeutic use