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PROGNOS: A Web-based Tool for Designing Engineered Nucleases

A web-based interface for Predicted TALEN Activity that effectively screens and reports potential unintended genomic targets.

Georgia Tech inventors have created PROGNOS, a web-based interface employing the Georgia Tech-developed Scoring Algorithm for Predicted TALEN Activity (SAPTA) that effectively screens and reports potential unintended genomic targets when designing TALENs and ZFNs, a capability not previously optimized for preparation of engineered nucleases. A user may enter sequence of a putative TALEN or ZFN, and PROGNOS searches a genome for off- target effects using the SAPTA algortithm. Users may also modify search specifications to cover mismatches for particular requirements. PROGNOS reports all genomic locations that might be susceptible to off-target cleavage and provides primers to amplify such regions for in vitro testing. In this manner, PROGNOS allows extraordinary streamlining of the process of designing and optimizing TALENs and ZFNs for numerous model organism knockout studies as well as therapeutic applications.

Summary Bullets

- Algorithm specifically prepared to search entire genomes to identify off-target cleavage sites and design optimal primers for TALENs and ZFNs
- Available as a simple, user-friendly web-based tool; no extraordinary bioinformatics or biochemical skill required
- Capable of analyzing TALEN and ZFN sequences targeting human, rat, mouse, zebrafish, arabidopsis, yeast, D melanogaster,

Solution Advantages

- Algorithm specifically prepared to search entire genomes to identify off-target cleavage sites and design optimal primers for TALENs and ZFNs
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- Capable of analyzing TALEN and ZFN sequences targeting human, rat, mouse, zebrafish, arabidopsis, yeast, D melanogaster,
- C elegans, Dog, Ape, Cow, Pig
- Algorithm validated against previous papers reporting off-site effects as well as in-house testing of reliability

Potential Commercial Applications

- Biomedical research
- Therapy of genetic disease
- TALENs and ZFNs

Background and More Information

Transcription Activator-Like Effector Nucleases (TALENs) and Zinc Finger Nucleases (ZFNs) are engineered proteins capable of genomic DNA cleavage to change or eliminate expression of proteins in metazoan animals. This technology has only developed in the last several years and is a critical capability for biomedical research and has applications for therapy of genetic disease. Despite high specificity, custom design of TALENs and ZFNs often results in tools that accidentally target inappropriate genes, resulting in incorrect research conclusions and precluding use in the clinic.

Inventors

- Dr. Gang Bao
  Former Georgia Tech Researcher; Foyt Family Professor in Bioengineering, CPRIT Scholar in Cancer Research, Associate Dean for Research and Innovation - Rice University George R. Brown School of Engineering

IP Status

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Publications

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Images

A. Enter Nuclease Half-Sites

5' ▭ 3'   5' ▭ 3'
3' ▭ 5'   3' ▭ 5'

B. TALEN Sites Entered in Red Boxes

5' GCACCTGACTCCTGT 3'   5' ▭ 3'
3' ▭ 5'   3' CGTGGACTGAGGACA 5'

C. Complementary Sequences Added to Blue Boxes

5' GCACCTGACTCCTGT 3'   5' GCACCTGACTCCTGT 3'
3' CGTGGACTGAGGACA 5'   3' CGTGGACTGAGGACA 5'

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