Docket #: S23-060

Translational Activators as Therapeutics for Protein Synthesis Diseases and Ribosomopathies

Stanford scientists have developed a high throughput screening method to identify therapeutics known as translational activators to treat protein synthesis disorders and ribosomopathies. Through this screen, they identified a novel function for the antibiotic Azithromycin and other macrolides that increase global protein production and rescue protein synthesis disorders in human cells in vitro, and in an in vivo mouse model.

Ribosomopathies are diseases that limit global protein production. Some examples are Diamond Blackfan Anemia (DBA) and amyotrophic lateral sclerosis (ALS). Current therapies mainly treat symptoms rather than the underlying pathobiology, leaving a large unmet need for patients. Stanford researchers have now developed a high throughput cell-based imaging screen that labels new proteins with fluorescent dyes. They have identified >200 translational activators with a proof of concept in disease models of DBA and ALS. Interestingly, they discovered FDA approved macrolide antibiotics such as Azithromycin can act as translational activators in human cells. Azithromycin is a safe, routine antibiotic widely utilized, and now Stanford scientists have demonstrated a novel function for Azithromycin that can treat the underlying cause for protein production disorders. This high throughput assay screens agnostic of mechanism and can repurpose clinically safe drugs such as Azithromycin for protein biosynthesis diseases.

Stage of Development
Proof of Concept – research, *in vitro* for the screening assay
In vivo proof of concept for Azithromycin to treat protein biosynthesis disease

Figure

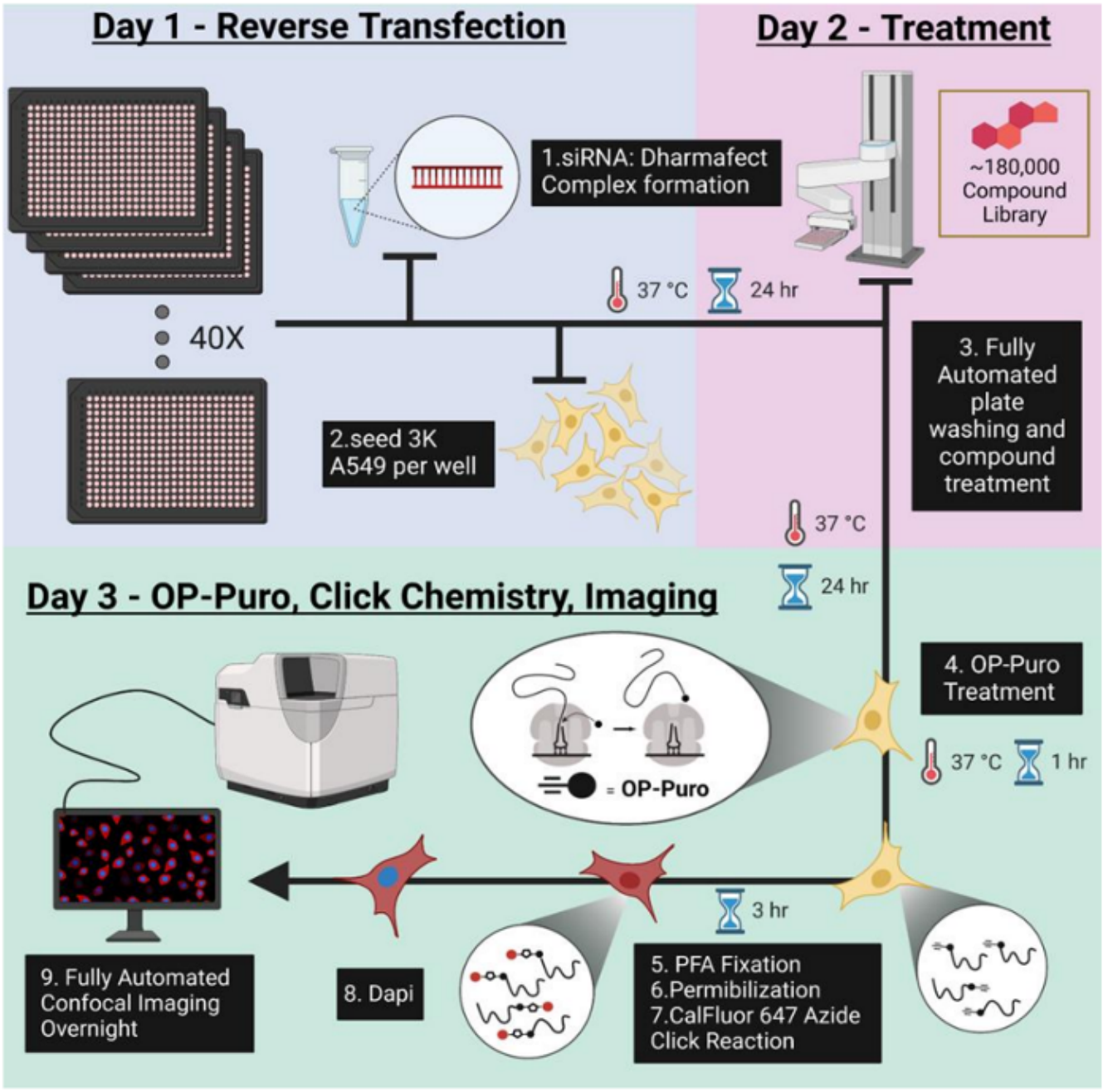

Figure Description: Workflow of the high-throughput cell-based imaging screen for identifying translational activators and potential therapies (source: inventors).

Applications

- Drug discovery for and treatment of protein synthesis or ribosomal diseases
- Drug discovery for haploinsufficiency
- Drug repurposing
- Protein biosynthesis modulators

Advantages

- High throughput
- Imaging based
- Novel mechanism of action
- Repurposing of approved therapies
- Low reagent cost
- Semi-automated

Innovators

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