

Successful delivery of CRISPR/Cas9 into cells *ex vivo*

- **Phylogica has successfully delivered CRISPR/Cas9 into cells *ex vivo***
- **The result establishes 'proof of concept' for the use of Phylogica's Cell Penetrating Peptides (CPPs) to deliver CRISPR/Cas9 into target cells**
- **Over the past week, we have identified highly promising 'second generation' CPPs that are very efficient at delivering cargo into the target cell of interest in this program**
- **We will now progress to obtaining a competitive read-out for these 'second generation' CPPs with results expected to be available in the first half of next year (this will inform the commercialisation prospects for the work)**

4 December 2018: Phylogica is pleased to advise that we have seen the first evidence of our ability to deliver the **CRISPR-associated protein 9 (Cas9)** using our Cell Penetrating Peptide (CPP) platform.

The results

We have used our 'first generation' CPPs to deliver Cas9 into the nucleus of a difficult to transfect cell line. Successful delivery of the Cas9 cargo has resulted in a 'knockdown' of the expression levels of a receptor on the surface of those cells as a result of the gene-editing achieved by the Cas9.

Next steps

The next steps in this body of work are to determine the optimal conditions for CPP-mediated Cas9 delivery. Once we understand these conditions (eg. how long should we incubate the CPP-Cas9 constructs on the cells, what is the optimal concentration of CPP-Cas9 to achieve maximum gene editing and minimum toxicity etc.) we can progress to a competitive read-out to assess the relative efficacy/safety of Phylogica's CPPs when compared to other delivery approaches for Cas9.

The ultimate read-out for this program will be conducted in primary cells (cells derived directly from a living organism rather than the immortalised laboratory cells used here) and will demonstrate the absolute numbers of cells that we are able to successfully achieve gene-editing in relative to alternative delivery approaches (eg. electroporation and lipid-based delivery systems). The primary cells used in this read-out will be the cell type of interest for the *ex vivo* commercial applications of the CRISPR/Cas9 technology and should therefore directly inform the commercialisation prospects for the program.

Second generation CPPs

In parallel to the testing of our 'first generation' of CPPs in the context of Cas9 delivery (described above), we have also identified and matured 'second generation' CPPs that are substantially more efficient at delivering cargoes into the target cell of interest in the Cas9 program. These CPPs have been ordered and will be available for evaluation in the CRISPR/Cas9 program in the first quarter of 2019.

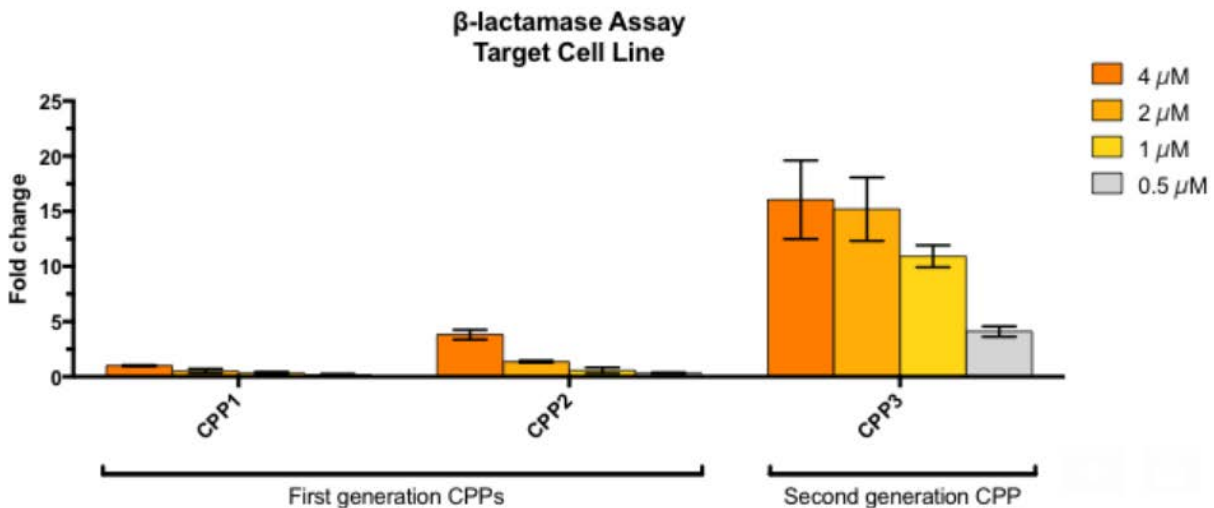


Figure 1: The relative delivery efficiency of the two 'first generation' CPPs (CPP1 and CPP2) that have the ability to deliver Cas9 into target cells *ex vivo* compared to the 'second generation' CPP (CPP3) that is yet to be tested with the Cas9 cargo. These results are from the same target cell that is of interest for this program. The chart shows the ability of each CPP to deliver the beta-lactamase cargo (an enzyme) into the target cell at four different concentrations. The 'second generation' CPP can deliver >10x as much cargo into the target cell as the 'first generation' CPPs.

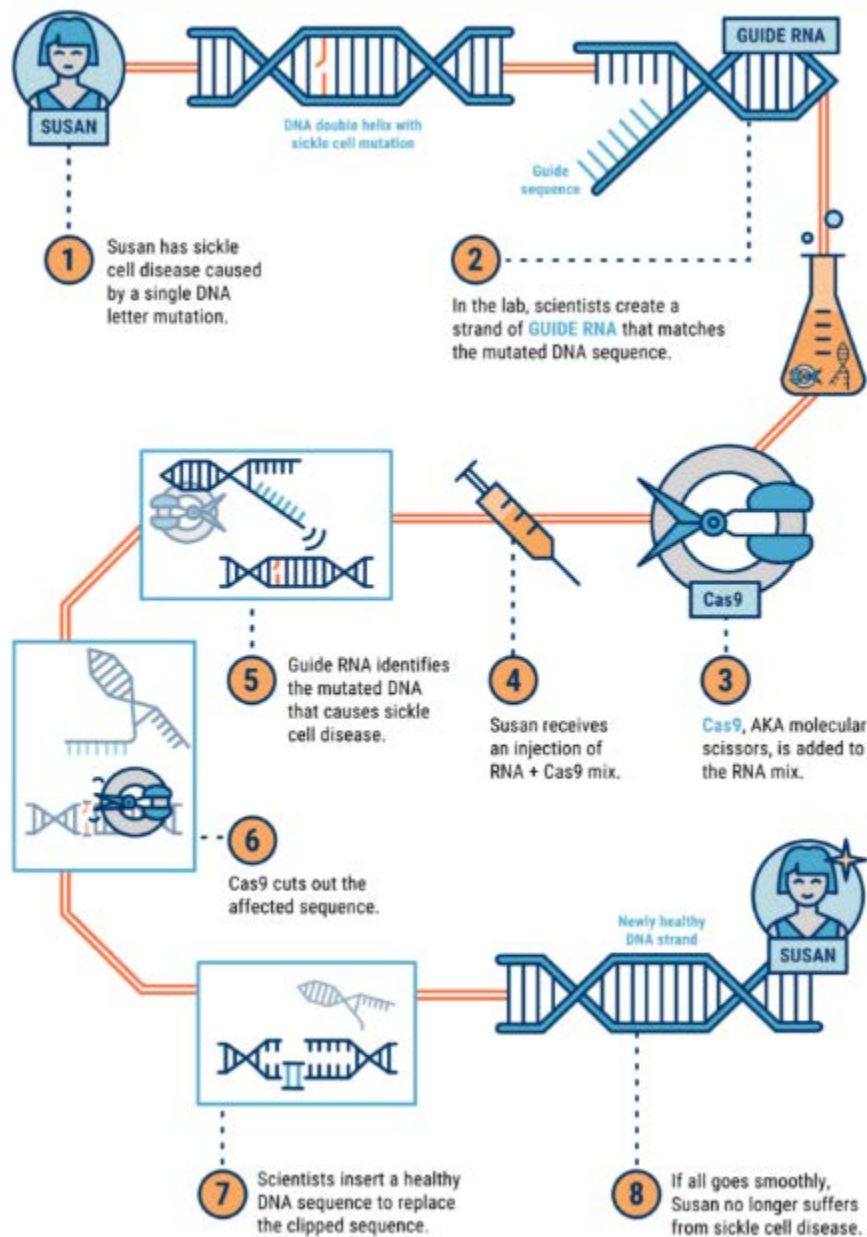
Background on CRISPR/Cas9

CB Insights recently published a helpful diagrammatic overview of the CRISPR/Cas9 technology (copied below).



What Is CRISPR?

UNDERSTANDING HOW THE CRISPR GENE-EDITING PROCESS WORKS



This is a simplification of the CRISPR-Cas9 treatment and is used for illustrative purposes.

CBINSIGHTS

Phylogica (ASX:PYC) is the owner of a peptide library containing the extraordinary richness and diversity of nature. We are using these libraries to develop a drug delivery platform capable of reaching the highest value drug targets located inside cells. Our delivery platform enables drug cargoes to cross the cell membrane and directly reach their target.

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About Phylogica

Phylogica Limited (ASX: PYC) is a biotech company focused on commercialising its intracellular drug delivery platform and screening its peptide libraries to identify drug cargoes for development against a wide range of disease targets. Phylogica controls access to the world's most structurally diverse source of peptides which have the ability to act as effective drug delivery agents and drug cargoes, penetrating cell walls to reach previously 'undruggable' targets across a range of disease types. Phylogica's platform of proprietary cell penetrating peptides has been validated across multiple animal models for the ability to deliver a diverse range of drug cargoes into cells. The company has collaborations with several pharmaceutical companies including Roche, Medimmune, Pfizer, Janssen and Genentech.

Forward looking statements

Any forward-looking statements in this ASX announcement have been prepared on the basis of a number of assumptions which may prove incorrect and the current intentions, plans, expectations and beliefs about future events are subject to risks, uncertainties and other factors, many of which are outside Phylogica's control. Important factors that could cause actual results to differ materially from assumptions or expectations expressed or implied in this ASX announcement include known and unknown risks. Because actual results could differ materially to assumptions made and Phylogica's current intentions, plans, expectations and beliefs about the future, you are urged to view all forward-looking statements contained in this ASX announcement with caution. Phylogica undertakes no obligation to publicly update any forward-looking statement whether as a result of new information, future events or otherwise.

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