Group work - Day 5

CRISPR genome engineering for cellular modelling and screening 2024

Matt Coelho and Kalpana Surendranath

Project groups

Group 1	Diana Adão
	César Bernat Silvestre
	Cecil Jack Weale
	Enoch Alex
	Sina Krokowski
Group 2	Heyne (Cecilia) Lee
	Elvira Hernandez-Gutierrez
	William Dalleywater
	Simon Ereh
	Zhe Yang
Group 3	Maqsood Chotani
	Sulagna Dasgupta
	Lorraine Southam
	Liliya Kopanitsa
	Luisa Giudici
Group 4	Vanessa Daza Cajigal
	Sanne Berkers
	Lai Ting Chan
	Shamjetsabam Nandibala Devi
	Philomena Hallford
Group 5	Omar Melo
	Svaty Sachania
	Maria Dudau
	Hannah Stabb
	Chunbo Yang
Group 6	Bo Fussing
	Marta Labeur
	Ekaterina Lashmanova
	Arnelle Edwards
	Valeria Di Leo

Objective

- Revisiting and consolidating your learning from days 1 to 4, the group work will provide an opportunity to design your study, from selecting the model to collecting and analysing data.

Methods, Strategies, and Justification

There are no “correct” answers here. Just justify your approach.

1. model

- Single nucleotide variant in the promoter
- Which CRISPR technology might you use?
- How will you design your gRNAs?
- Which cell type?
- How might you validate the engineered cell model?

2. screen

- What gRNA library might you use?
- Which controls will be important to include
- What will your screen readout be and how will you measure this?

3. analysis

- What normalizations would be relevant for the sequencing data?
- Which statistical approach might you use to analyse the screen?
- Describe any validation or next steps

Structuring your work

- This is a 10-minute group presentation with 5 minutes allocated for questions.
- You may emphasize one or more categories (Model, Screen, and Analysis) in your discussion.
- The presentation can be delivered by all team members or by a selected representative

Scenario

- A mutation in the promoter of the gene *B2M* has recently been found to alter the expression of B2M, a cell surface protein. This leads to an uncommon blood disorder.
- The presence of the mutation does not always lead to disease, suggesting there are other factors at play. Your research team has been tasked with identifying genes involved in disease progression - particularly new drug targets to reverse the blood disorder.

1. Describe a CRISPR-based workflow to introduce the promoter mutation in *B2M* in a cell model.
2. Describe how you would design a CRISPR KO screen to identify modulators of *B2M* expression in this modified cell model.

- **For each step, give a rationale for your approach and describe the analysis in each case.**