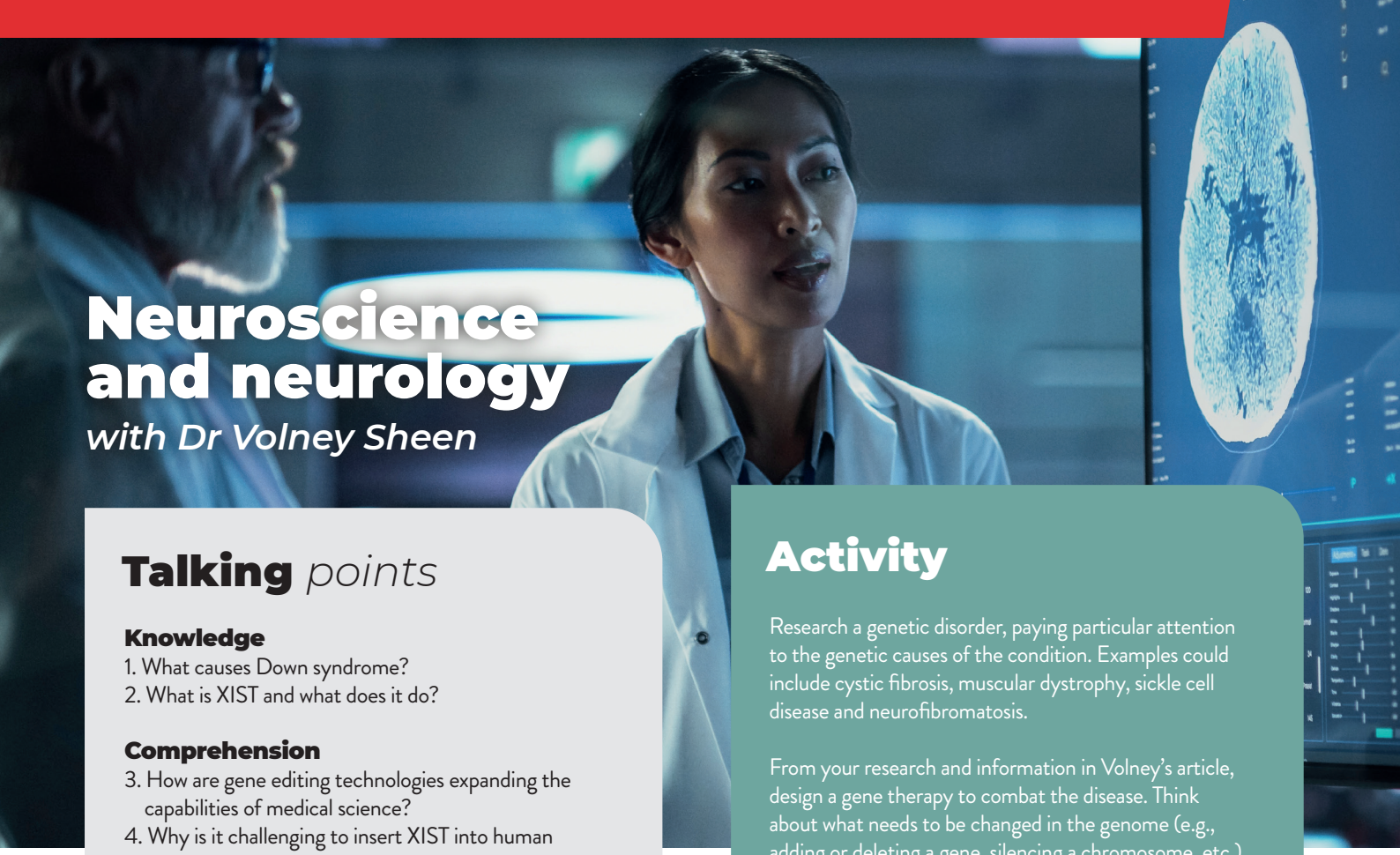

Neuroscience and neurology

with Dr Volney Sheen

Talking *points*

Knowledge

1. What causes Down syndrome?
2. What is XIST and what does it do?

Comprehension

3. How are gene editing technologies expanding the capabilities of medical science?
4. Why is it challenging to insert XIST into human chromosomes?

Application

5. What questions would you ask Volney and the team to learn more about the different applications of tissue cultures and mice models for testing gene therapy techniques?
6. Mice have 20 pairs of chromosomes, meaning they do not have chromosome 21. What do you think is meant by 'the mouse equivalent of Down syndrome'?

Analysis

7. In females, XIST silences one copy of the X chromosome, but not both. Why do you think it is important for the team to understand how this happens, and how could they apply this knowledge to their work using XIST as a therapy for Down syndrome?
8. Why would prenatal gene therapy be more effective than postnatal gene therapy?

Evaluation

9. Despite having health issues, many people with Down syndrome live full and rich lives if they have the right support systems in place. Because of this, some people are wary about seeking 'cures' for the disorder. How do you think that society should approach Down syndrome in the most ethical and compassionate way?
10. Gene therapy has almost-limitless potential: in theory, it could be used with embryos to not only eliminate genetic diseases but also determine physical and mental characteristics. Where do you think the limit should be drawn, from an ethical standpoint? And how do you think society will respond as these technologies become more advanced?

Activity

Research a genetic disorder, paying particular attention to the genetic causes of the condition. Examples could include cystic fibrosis, muscular dystrophy, sickle cell disease and neurofibromatosis.

From your research and information in Volney's article, design a gene therapy to combat the disease. Think about what needs to be changed in the genome (e.g., adding or deleting a gene, silencing a chromosome, etc.), how CRISPR-Cas9 gene editing technology could help achieve this, and how the therapy could be delivered to patients. What experiments could scientists conduct in the lab to assess whether your gene therapy could be effective? What challenges would they need to overcome to move their research from the lab into clinical trials in humans?

Once you have designed a potential gene therapy, conduct further research to explore whether any gene therapies (or other treatments) currently exist for the condition. If so, how similar are real treatments from your idea? If not, what challenges are scientists trying to overcome to develop suitable treatments?

More *resources*

- Visit Volney's lab website to learn more about his research: **research.bidmc.org/volney-sheen**
- This video explains the first roll-out of CRISPR-Cas9 into clinical practice, to treat sickle cell disease: **youtube.com/watch?v=uHWD8RSw4As**
- This article provides an accessible introduction to how gene editing can be used to cure disease: **sciencejournalforkids.org/articles/how-can-gene-editing-cure-disease/**
- This article introduces the work of other researchers using gene therapy to prevent Down syndrome: **reuters.com/business/healthcare-pharmaceuticals/health-rounds-gene-editing-may-hold-key-preventing-down-syndrome-2025-02-19/**