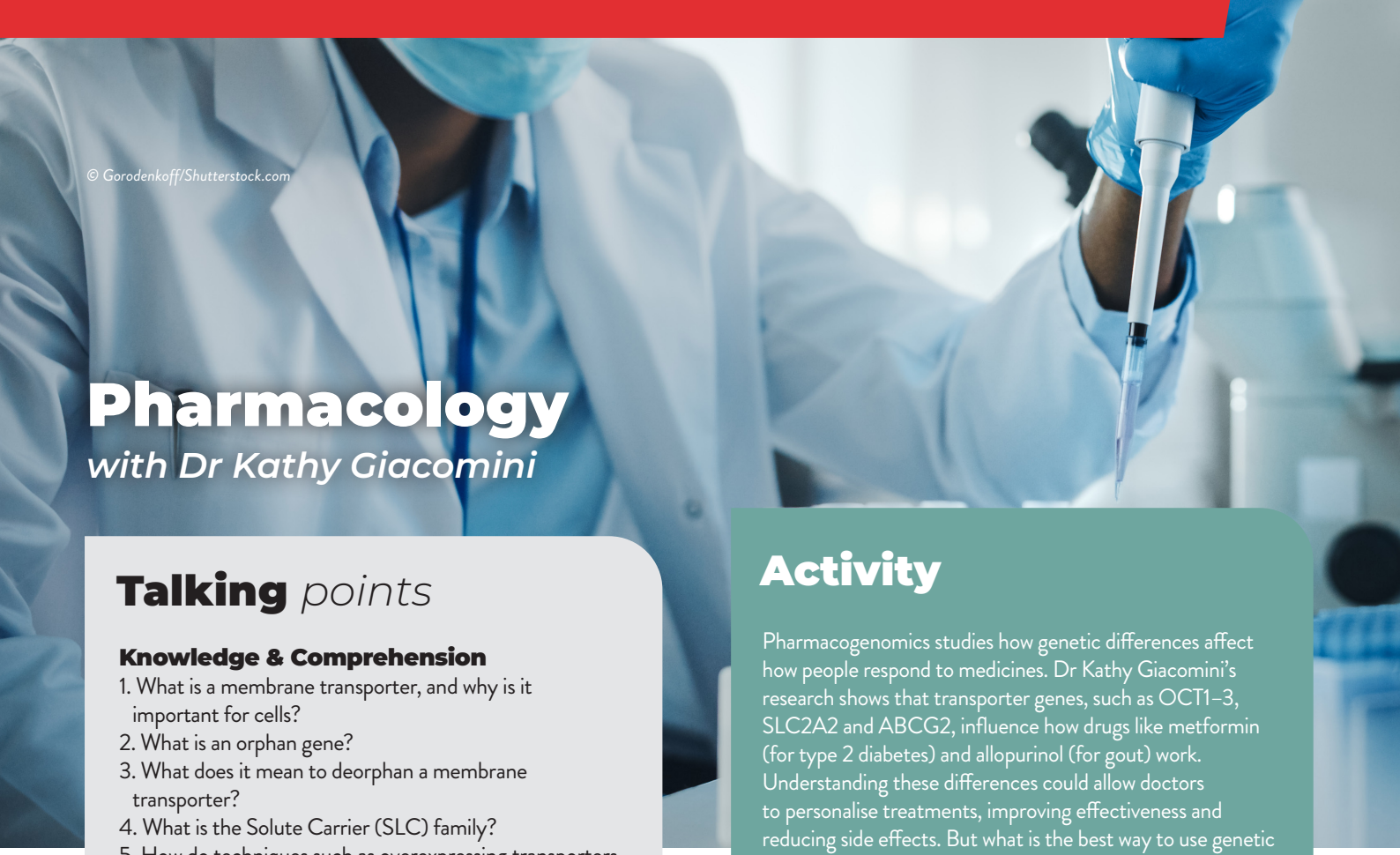

Pharmacology

with Dr Kathy Giacomini

Talking *points*

Knowledge & Comprehension

1. What is a membrane transporter, and why is it important for cells?
2. What is an orphan gene?
3. What does it mean to deorphan a membrane transporter?
4. What is the Solute Carrier (SLC) family?
5. How do techniques such as overexpressing transporters in cells, metabolomic genome-wide association studies and confocal microscopy help scientists figure out what an orphan transporter does?
6. How does the stop-codon variant in SLC22A24 influence how the kidney handles androsterone glucuronide?

Application

7. How might discovering the substrates of orphan transporters help improve the safety and effectiveness of existing medicines?
8. How could knowledge about transporter variants be applied in personalised medicine to predict how different patients will respond to the same drug?

Analysis

9. Why might highly promiscuous transporters in the SLC22 family be more difficult to study than highly specific transporters such as the dopamine transporter?
10. How do the evolutionary changes seen in transporters like SLC22A10 and SLC22A24 illustrate the relationship between genetics, physiology and human evolution?

Evaluation

11. Kathy and her research team use clinical studies, evolutionary analyses and molecular experiments to study transporter function. To what extent does combining multiple scientific approaches strengthen discoveries in pharmacology, and why?
12. Humans have lost the function of SLC22A10, which is still active in chimpanzees. What might this tell us about how evolution shapes biology, and what could be the consequences of losing certain transporters over time?

Activity

Pharmacogenomics studies how genetic differences affect how people respond to medicines. Dr Kathy Giacomini's research shows that transporter genes, such as OCT1–3, SLC2A2 and ABCG2, influence how drugs like metformin (for type 2 diabetes) and allopurinol (for gout) work. Understanding these differences could allow doctors to personalise treatments, improving effectiveness and reducing side effects. But what is the best way to use genetic information to guide medicine?

1. Divide into small groups: each group will act as a team of pharmacologists that will receive five fictional patient case studies. First, create your patient case studies, and for each profile include:
   - Age, sex and condition (e.g., type 2 diabetes or gout)
   - A genetic variant in a transporter gene (OCT1–3, SLC2A2 or ABCG2)

2. Consider drug response for each patient:
   - What might influence how a patient responds to a standard drug dose?
   - To what extent is it possible to predict an individual patient's response to a drug, and why?
   - How might the genetic variant increase or reduce drug uptake, affect metabolism, or change elimination?

3. Suggest personalised treatment adjustments:
   - Think about whether you should, for example, adjust the dose, switch to a different drug, or monitor the patient more closely.
   - Write a short explanation for each decision.

4. Reflect and discuss:
   - What are the ethical issues with research in this area, and how might they be addressed?
   - How could pharmacogenomics improve patient care and reduce adverse drug reactions?
   - What challenges might healthcare professionals face when using genetic information to guide prescriptions?
   - To what extent should personalised medicine replace standard treatment guidelines?
   - How might society balance access, cost and ethical concerns when using genetic testing to guide medicine?