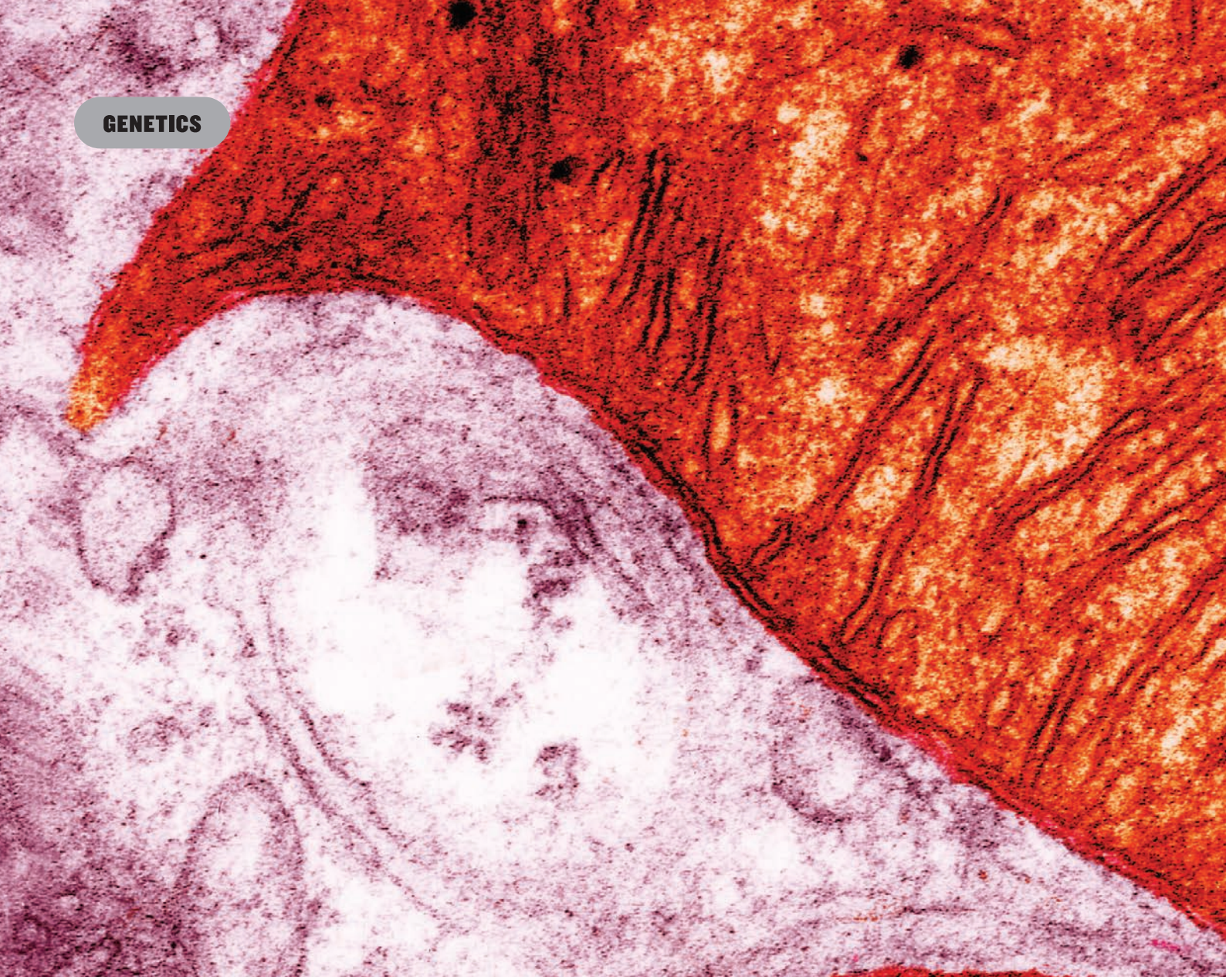
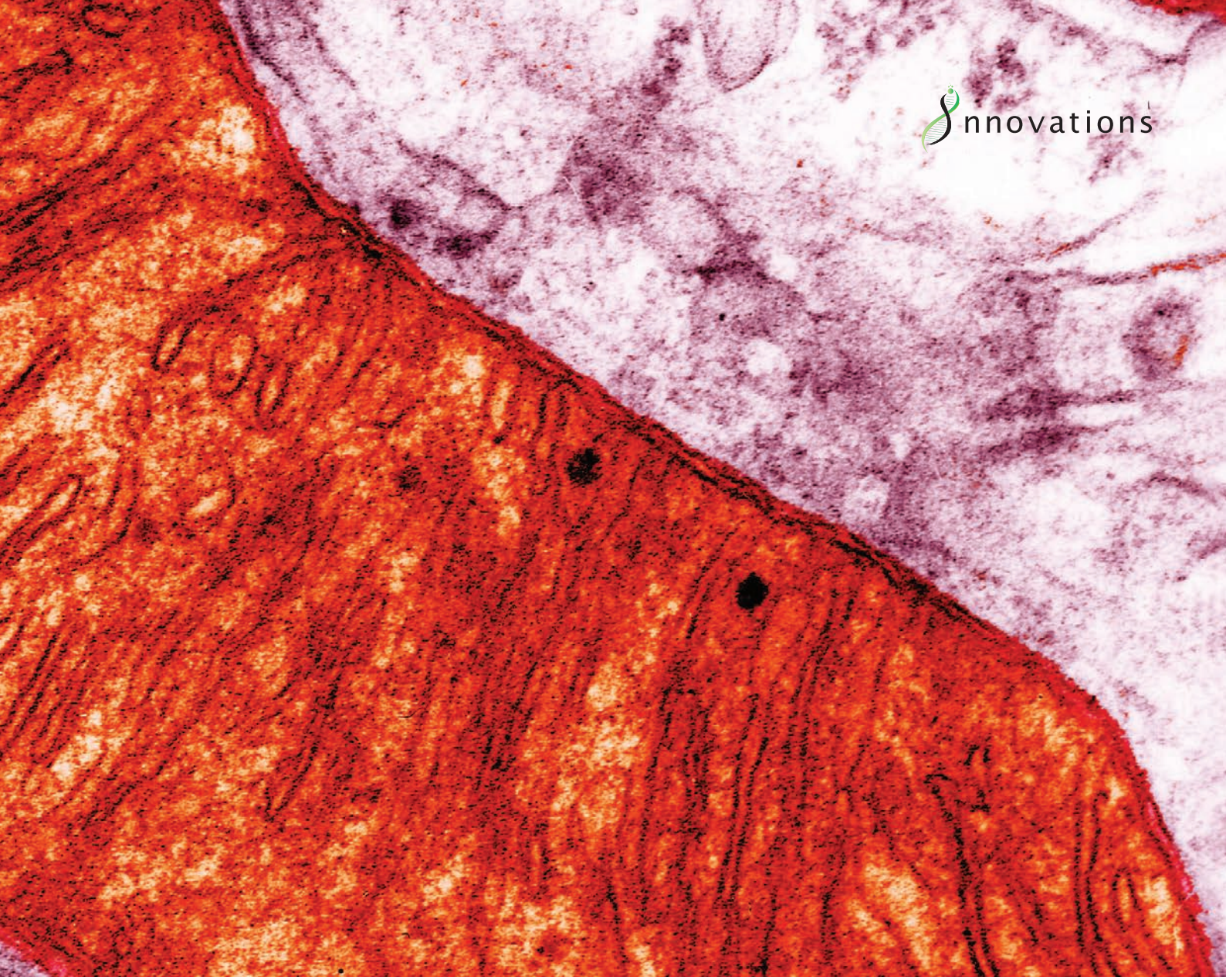


The many faces of a mitochondrial mutation

A rare gene mutation affecting a mitochondrial transporter could be more common than previously thought.

A team of Saudi researchers has found that a rare genetic mutation, mainly affecting the brain and muscles, may be more common than previously thought because it presents differently in people. The team studied 12 patients from Saudi Arabia and the US with a mutation in the gene SLC25A42. They found that each patient carried the same 'founder mutation' but that its clinical presentation varied.

SLC25A42 codes for a protein that binds to and transports a crucial compound, called coenzyme A, across the membrane of mitochondria, the energy powerhouses of cells. Many enzymes need this compound to catalyse some of the most crucial reactions of metabolism. The disease associated with mutations in this gene is



Mitochondria are the energy-supplying powerhouses of the cell, but are significantly disrupted by mutation in the SLC25A42 gene.

BSIP SA / ALAMY STOCK PHOTO

a form of 'mitochondrial encephalomyopathy', with a range of neurological and muscular problems as its most obvious clinical manifestations.

The apparent absence of neurological problems in one child with the SLC25A42 mutation was the clue that led the research team to discover that the overall effects of the mutation can be more variable than previously supposed. The researchers identified twelve patients with the mutation by examining their medical histories. They then examined the protein-coding portions of their genomes. Their analysis revealed that the same mutation led to varied clinical manifestations, ranging from very mild, barely noticeable symptoms, to severe developmental impairment and epilepsy.

"Given the variable severity and non-specific presentation, this disorder is probably underestimated," the researchers conclude in their study published in the journal Clinical Genetics. They suggest that clinicians should be more aware of the possibility that this disorder may lie behind any of a range of symptoms they have reported. They also suggest this should be considered "especially in patients of Arab descent," given the prevalence of births from closely related parents in that population. Consanguinity was a common factor in the 12 cases examined in this study.

Almannai, M., Alasmari, A., Alqasmi, A., Faqeih, E., Al Mutairi, F. et al. Expanding the phenotype of SLC25A42-associated mitochondrial encephalomyopathy. *Clinical Genetics* **93**, 1097-1102 (2018).