The Science Communication Competition is now in its fifth year. As in previous years, it aims to find young talented science writers and give them the opportunity to have their work published in *The Biochemist*. In 2015, a new branch of the competition was launched to include video entries. Overall this year's competition attracted 47 entries and these were reviewed by our external panel of expert judges. The first prize in the written category was awarded to Emma Yhnell from Cardiff University, whose article is presented here; the winner of the video category was Chris Morgan from the University of Birmingham.
Chris Morgan's winning video can be viewed on the Society's website: http://bit.ly/1kxt8eH

James and the Giant Gene

Emma Yhnell
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I'd like you to meet James, he is a pretty normal chap. He works hard all week and looks forward to spending his weekends with his wife and two children.

But recently James has been feeling a bit down. He has been getting really moody with his family, he is lacking in motivation at work and he has had a few stumbles and falls around the house. After a few months of nagging from his wife, James booked an appointment to discuss his health with his doctor. James was adopted as a child, so he didn't know of any medical conditions that ran in his family. The doctor referred him to a neurologist to investigate his symptoms further.

After many weeks of tests and investigations, James was called in to see a neurologist for his results. He received some life-changing news that would affect him and his family for the rest of their lives. "I'm sorry to have to tell you that you carry the gene for a rare brain condition known as Huntington's disease and you are exhibiting some of the early symptoms. We can give you some treatments to control your symptoms but unfortunately, they will worsen over time and there is currently no cure."

James did not know what to say. Finally, he had a name for what was causing the troubles that he had been experiencing for the past few months. But he also had so many unanswered questions. What had caused his disease? Could he have passed the disease on to his children?

The gene that causes James's disease was discovered over 20 years ago. Scientists know that DNA contains the letters C, A, G and T which are arranged to spell genes, and these genes form proteins which are essential for the body to function properly. Everyone, including you and I, has a huntingtin gene, which is required for normal growth, development and health. The huntingtin gene contains a region of CAG letter repeats. Most people have a huntingtin gene with a small number of CAG repeats, normally between 10 and 35. But, people like James, who have Huntington's disease, typically have over 40 CAG repeats within their huntingtin gene. The genetic region with the CAG letters has been misspelt with too many CAG letters. It has expanded, creating a bigger gene, a giant gene, which creates an abnormally big, abnormally functioning protein.

The giant gene creates a long strand of huntingtin protein which, like the chain of a necklace, becomes tangled and knotted within the cells of the brain. These knotted clumps of huntingtin protein are called aggregates. There is a great amount of dispute about the function of the huntingtin aggregates. Some researchers think that aggregates are toxic, whereas others think that the formation of aggregates may be a protective mechanism. However, it is known that the build-up of huntingtin aggregates in the brain interrupts the chemical messages that control the body and mind and ultimately cause brain cells to die. This means that people with Huntington's disease experience a range of symptoms, which affect all areas of their lives. Symptoms often begin with relatively subtle, but troubling, behavioural changes such as depression, anxiety and sleeping problems. These symptoms typically worsen and become more physically disabling causing shaking, mobility problems and lack of ability to eat. By the end stages of Huntington's disease, often 10–15 years after diagnosis, people become very disabled and need constant care.

James and his wife were given the opportunity to see a genetic counsellor to discuss the implications of his diagnosis. He was told that the disease generally begins to affect people in their thirties and forties. The disease is heritable, as a person with Huntington's disease has one faulty copy of the huntingtin gene and one good copy. This means there is a 50% chance the children of a person with Huntington's disease could inherit the condition; one of James's birth parents may have had a faulty copy of the huntingtin gene and passed it on to him. James's could have unknowingly passed the faulty huntingtin gene on to his children, and they can choose to be tested for it once they are 18 years old.

Although we know the genetic cause of Huntington's disease, we have not yet been able to cure it. This is because the molecular and biochemical processes that cause the disease are yet to be fully understood, as the

size of the long tangled protein created from the giant gene makes it hard to study. However, we do know that the protein which causes Huntington's disease is produced from a spelling mistake in the huntingtin gene, and if we can get rid of the giant misspelled protein then we might be able to prevent Huntington's disease. Current research is focusing on using molecular techniques which prevent the formation of the giant huntingtin protein, to potentially improve the symptoms experienced by patients with Huntington's disease.

One potential treatment for Huntington's disease is to use small interfering RNA (siRNA) molecules, which are synthetically created to prevent proteins forming. Genes contain letters which need to be copied to spell out and create proteins. A bit like Tipp-Ex®, siRNAs are used to cover the copy of the 'wrongly' spelt genes so that the letters that spell the gene cannot be used to form proteins. siRNAs have been designed to bind to the copy of the giant huntingtin gene and prevent the formation of the abnormal protein. If the giant misspelled huntingtin protein can't be formed this could prevent the disease from occurring, and the symptoms experienced by patients with Huntington's disease may be improved. More research and development is required before siRNAs can be used as a possible treatment option for Huntington's disease, but it is one option being investigated by researchers.

As well as looking in to possible treatments, we also need to better understand why the huntingtin gene causes Huntington's disease. It is hoped that ongoing research in to this will improve the lives of people such as James who are currently living with Huntington's disease, and for the many thousands of people who may go on to develop this devastating neurological disease. ■

Some resources and further information

The Huntington's Disease Association (http://hda.org.uk/)
HDBuzz (http://en.hdbuzz.net)

Selected recent reviews and research into Huntington's disease and triplet repeat genetic disorders:

Schiefer, J., Werner, C.J. and Reetz, K. (2015) Clinical diagnosis and management in early Huntington's disease: a review. *Degenerative Neurological & Neuromuscular Disease* **5**, 37–50
Bates, G.P., Dorsey, R., Gusella, J.F. (2015) Huntington disease. *Nature Reviews Disease Primers* doi:10.1038/nrdp.2015.5
Mason, S. and Barker, R.A. (2015) Progress in Huntington's disease: the search for markers of disease onset and progression. *Journal of Neurology* doi:10.1007/s00415-015-7700-0
Sanders, S.S. and Hayden, M.R. (2015) Aberrant palmitoylation in Huntington disease. *Biochemical Society Transactions* **43** 205–210
Iyer R.I., Pluciennik, A, Napierala, M., and Wells, DF (2015) DNA triplet repeat expansion and mismatch repair. *Annual Review of Biochemistry* **84**, 199–226
Olejniczak, M., Urbanek, M.O. and Krzyzosiak, W.J. (2015) The role of the immune system in triplet repeat expansion diseases. *Mediators of Inflammation* doi:10.1155/2015/873860
Richard, G.-F. (2015) Shortening trinucleotide repeats using highly specific endonucleases: a possible approach to gene therapy? *Trends in Genetics* **31**, 177–186

The annual Science Communication Cpmpetition is open to talented science communicators who can be undergraduate or postgraduate students; both members of the Society and non-members. Entries to in the written and video categories must be original works on a molecular bioscience topic and be targeted at the general public. Full details of the competition, including past winners and terms and conditions are available at http://bit.ly/1kxt8eH