This case study was one of two runners-up in BBSRC's Impact Writing Competition 2019. The competition invited PhD and early-career researchers to submit a case study showcasing social or economic impact arising from BBSRC investments, providing experience of writing about science for a policy audience. This entry was written by Elizabeth Hampson, a PhD student at the Babraham Institute, one of BBSRC's strategically funded institutes.

The Ageing Clock at the Babraham Institute *by Elizabeth Hampson.*

Eternal life and the quest for immortality have been of interest to humans for centuries; we want to live healthier and for longer and have a vested interest in how and why we age. 200 years ago the average human would not make it to their 40th birthday, but now we can expect to reach our mid-80s. Research at the Babraham Institute, funded by the BBSRC, focuses on healthy ageing and exciting work on epigenetics from Wolf Reik's group has the potential to revolutionise how scientists study ageing.

What is epigenetics?

DNA is the code which contains all the necessary instructions for life. Almost all cell types in your body contain an exact copy of your unique code, but they become many different types of cells. Some become muscles cells, whereas some form your brain. A scientific question to address is how does each cell know what to become if the instructions are all the same? This is like having the same set of instructions for flat pack furniture, but being able to build a bed, a desk and a chair.

Scientists have discovered that small tags are able to attach to DNA to switch genes on or off, and this is called epigenetics. Cells are able to specialise and gain different functions without altering the DNA code itself by switching these genes on or off using the epigenetic tags.

DNA methylation is one of these epigenetic processes, where the tag is a methyl group. This is critical for the growth of healthy mammalian cells.

The Epigenetic Clock

Here at the Babraham Institute in Cambridge, Wolf and his group have identified an epigenetic clock in mice. This work was published in Genome Biology in April 2017 in collaboration with the European Bioinformatics Institute. The epigenetic clock is a computer model that uses DNA methylation patterns to predict the biological age of a mouse. This predicted biological age can be compared to the chronological age (age since birth) and comparing the two ages can tell us whether the mouse is ageing in a healthy way.

The model uses changes at only 329 points out of a possible 23 million places on the DNA. Amazingly, these predictions are accurate to within 3.3 weeks of a mouse's 3 year life.

How will this help scientists study ageing?

The epigenetic clock will allow investigations into the mechanism of ageing. By comparing biological age with chronological age we can start to understand how different factors might influence the speed of the ageing process, for example alcohol, obesity, different diets, or exercise.

Studies have already shown, using the epigenetic clock that removing the ovaries from female mice can increase the rate of ageing, which could be useful for understanding the early menopause in women.

Additionally, diets with high levels of fat also accelerate the ageing clock, giving us new insights into society, health and our environment.

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What does this research mean for scientists at the Babraham Institute and further afield?

Ageing is a very long term process and is hard to measure and understand. Compounding the problem is the fact that ageing has different effects for different people, and even in different parts of one person's body. This makes processes like running a clinical trial for an anti-ageing drug exceedingly difficult as the ageing process is so slow. Now the epigenetic clock could be used as a reliable method to measure the rate of ageing over shorter timescales in mice, making these kind of studies a reality.

With further refinement, it could be possible to experimentally look at changes to our biology in response to ageing. As scientists have already started to do, we can study diet, drugs and their effect on rate of ageing in laboratory animals without having to invest the time in waiting for said animal to reach an advanced age. This makes research of this nature faster and more humane, and has the potential to revolutionise the kind of research into healthy ageing that is a priority at the Babraham Institute. Presently, to study ageing mice at the institute we often wait until they are 2 years in order to perform experiments, as this is when physiological signs of ageing are present. By using the epigenetic clock, changes can be seen as early as 9 weeks into the 3 year life of the mouse. Being able to perform these experiments earlier will make them increasingly more ethical.

What does this research mean outside of academia?

The reach of this work begins with the "Race Against the Ageing Clock" exhibit developed in collaboration with the public engagement team at the Babraham Institute. This appealing activity showcased at the 2018 Royal Society Summer Science Exhibition as a hands-on display for members of the general public of all ages to learn about the epigenetic clock and have the opportunity to talk to scientists from the Babraham Institute about the study of healthy ageing.

The research from Wolf's lab has already given rise to a company called Chronomics Ltd., co-founded by Tom Stubbs, the PhD student in Wolf's lab responsible for this work. Chronomics uses epigenetic measurements from saliva samples to give customers information and feedback on their health. Customers have access to "apps" for a variety of indicators of health, before being given information about each of these, the impact it will have for them, and what they can do to improve their health. This is a direct impact from BBSRC funded research to a start-up Cambridge based company, contributing financially and culturally to the UK business and health sectors.

Epigenetics also has an impact for cancer research in the pharmaceutical industry. There are multiple things that can go wrong in cancer that are driven by changes in epigenetics, it's often not as simple as mutations in our DNA. Some genes, called tumour-suppressor genes, help defend us against cancer. In some cancer patients these have been inactivated by epigenetic changes. What is exciting to academic researchers, and the pharmaceutic industry alike, is that epigenetic changes are reversible allowing drugs to be developed to reactivate these important defence genes. There are currently drugs in clinical trials for myelodysplastic syndrome, a type of blood cancer building on the understanding of epigenetics in cancer, driving forward the cancer research field.

Research into the epigenetic clock will hopefully lead to a better understanding of how humans could live healthier for longer. Life expectancy has risen sharply over recent decades, but many people live their later years in poor health. This discrepancy between increases in life expectancy and healthy lifespan has a big impact on our society, including resources such as the NHS, care workers and public transport. The robust investment of public money in healthy ageing research by the BBSRC comes full circle to improve the lives of UK citizens and shapes the current and future society we live in.

Exciting work on epigenetics from at the Babraham Institute has the potential to revolutionise how scientists study ageing. Image: The Babraham Institute.