

Science Communication Competition

The Science Communication Competition is now in its sixth 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 62 entries and these were reviewed by our external panel of expert judges. The third prize in the written category was awarded to **Jessica Hardy** from the University of Oxford, whose article is presented here; the third prize in the video category went to **Johanna Laibe** from Kingston University.

Johanna's video can be viewed on the Society's YouTube channel: <http://bit.ly/2c2dFmB>

Cancer: a disease of bad luck, or bad lifestyle?

Jessica Hardy
(University of Oxford, UK)

Cancer. It's an emotive word, and a dreaded diagnosis. We all know someone affected by this horrible disease, and quite understandably, we all want to know: what causes cancer, and is there anything we can do to stop ourselves from getting it?

This is one of the most burning public health questions of modern times, but it's pretty difficult to find a clear answer. Take these two headlines, both published on the BBC News website in 2015^{1,2}, and both based on scientific studies:

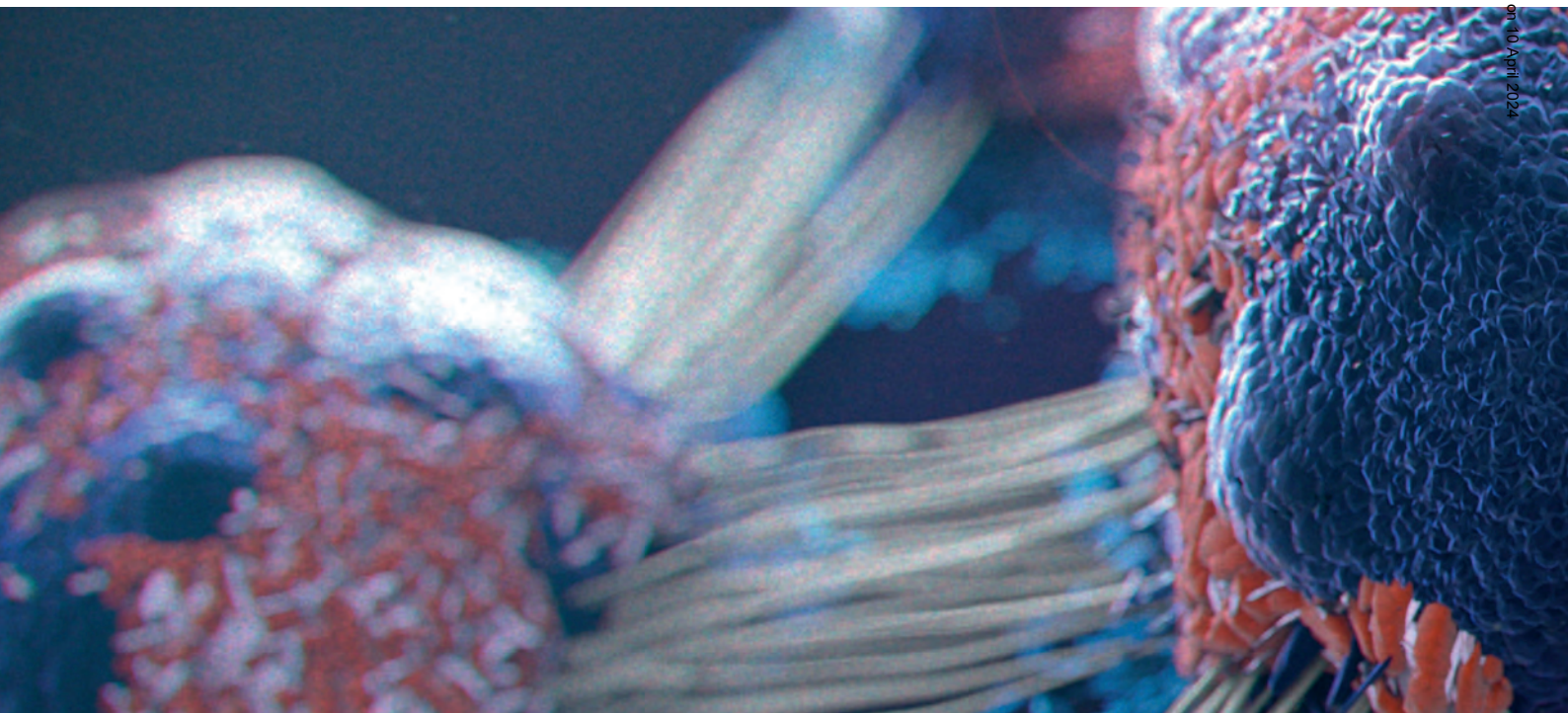
Headline 1: Most cancer types 'just bad luck'¹

Headline 2: Study suggests cancer is not 'just bad luck'²

So, which one is it? Can we throw caution to the wind, keep the 40-a-day smoking habit and indulge

in a daily fry-up, knowing that our risk of getting cancer is beyond our control? Or, can we completely eliminate our cancer risk by filling our lives with superfoods and daily workouts?

As you've probably guessed, the answer lies somewhere between these two extremes. There is clearly some element of 'bad luck' in developing cancer. Take Joe and Mike, who are both 61. Joe has never smoked, but sadly he's just been diagnosed with lung cancer. Mike has smoked heavily for 45 years, but remains healthy. This might seem unfair, and supports the idea that Joe's cancer is 'just bad luck.' However, it's well-established that smokers



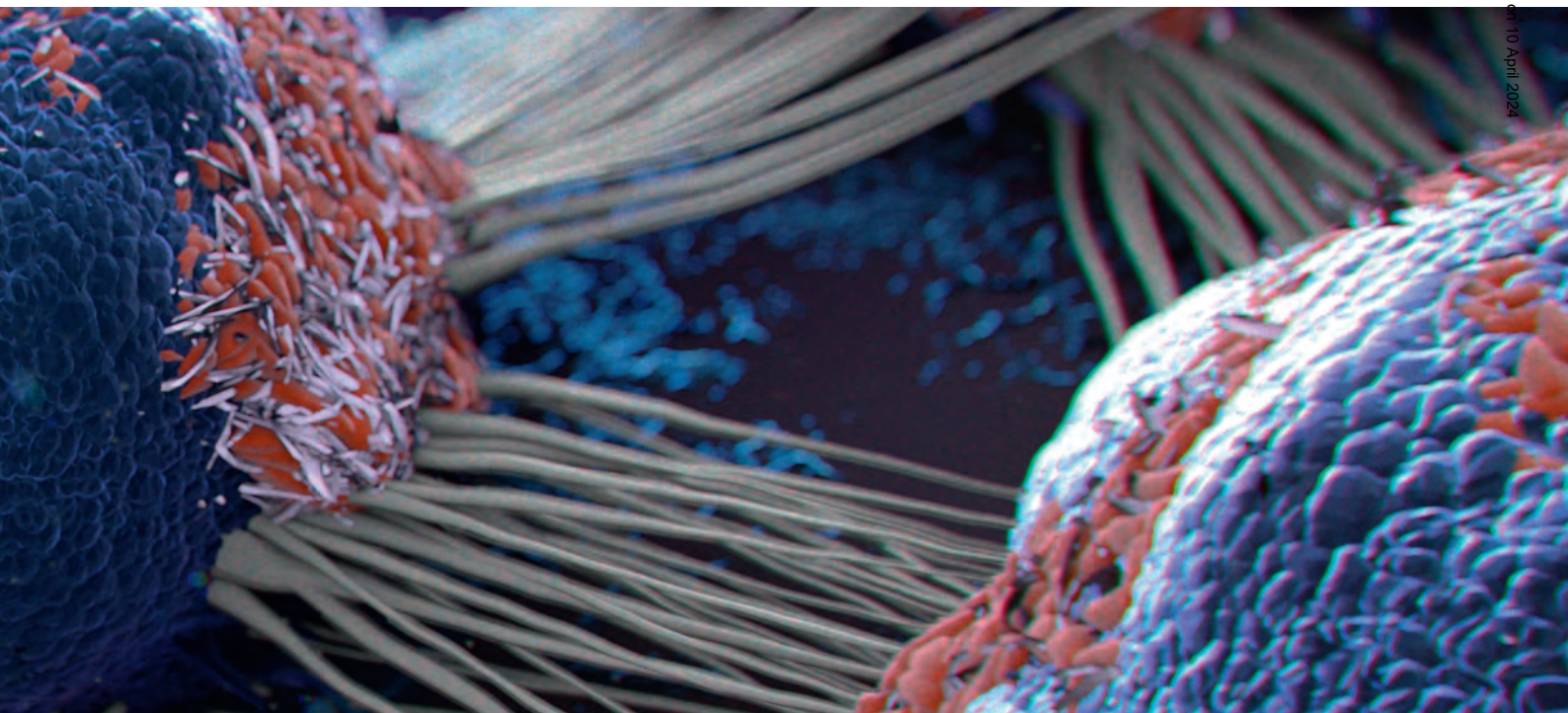
are much more likely to develop lung cancer than non-smokers and it would be unwise to completely dismiss the influence of lifestyle on cancer risk.

But just how much of cancer is about bad luck, and how much control do we really have? To tackle this question, it's important to understand how cancer develops. Cancer is, in short, a disease caused by excessive division of cells. Cells are the functional building blocks of our tissues and organs, and in order to grow, and to repair or replenish parts of these tissues, we need to be able to make new cells. Our bodies do this by using existing cells as templates for new ones, in a process called cell division. However, if cells divide when it's unnecessary, this can be problematic. It can lead to an overgrowth of cells, forming a tumour – a mass of rogue cells which don't work properly, and which disrupt the function of the affected organ. Left unchecked, these deviant cells ultimately evolve the ability to spread within the body and seed new tumours, eventually damaging vital organs and causing death.

The question is, then, what makes cells start to misbehave and divide when they shouldn't? The key lies in our DNA. Every cell contains a genetic code, made of a chemical called DNA, which contains the instructions that make the cell work correctly. This includes, for example, the code to make molecules which regulate cell division. The problems begin when this code is altered in some way – a process called mutation. Mutation can be thought of as miscopying or changing the code, much as someone might make a mistake when typing up a handwritten document. Let's imagine a secretary, Bruce, typing up some meeting notes. He's usually very accurate, but occasionally a mistake creeps in. This might

be harmless, and might not change the meaning of the sentence. For example, he might type 'We must not DISPOZE of hazardous waste in the yellow bin' instead of 'We must not DISPOSE of hazardous waste in the yellow bin'. Ok, he misspelt a word, but it doesn't really matter. Sometimes, though, the mistake might have dangerous consequences. He might type 'We must NOW dispose of hazardous waste in the yellow bin', rather than 'NOT'. That will cause trouble! The same can be said for copying the DNA code into a new cell during cell division. When representing the DNA code, we use 4 letters – A, T, C and G – to signify the 4 chemical bases of DNA. A 'T' in the code could, for example, be miscopied as a 'C'. Depending on which part of the code is affected, this may have little effect on the instructions, or it might completely change the behaviour of the new cell.

These DNA mutations happen very occasionally, by chance, every time a cell divides. This represents the 'bad luck' aspect of cancer. If enough chance mutations accumulate in important places in the DNA, enough instructions might be changed to make a cell divide continually or develop characteristics that support tumour growth – the so-called 'hallmarks of cancer'³. However, there are many factors which can increase the chance of these mutations arising. Let's consider Bruce's typing again. If he types his notes after having a few pints of beer, or after getting only 2 hours of sleep, he's much more likely to make mistakes. Analogously, smoking, the most notorious risk factor for cancer, greatly increases the chance of DNA mutations, as the chemicals in cigarettes can directly react with DNA, leading to changes in the code. Equally, too much sun exposure greatly increases skin cancer



risk, because UV light induces chemical reactions within DNA that can alter the code.

You may be wondering why then, if we understand how mutations can arise and lead to cancer, there are still such conflicting reports on how much of cancer is 'bad luck'.

The article entitled 'Most cancer types 'just bad luck'¹ was based on a study which addressed the question of why some organs, like the bowel, are more prone to cancer than others, like the brain⁴. The researchers found that this was partly explained by the number of dividing stem cells in each organ. The bowel is constantly renewing its lining, and therefore has lots of cell division, whilst brain cells divide much less frequently. More cell division and copying of the DNA means more chance for mutations to be introduced by miscopying. The authors used mathematical models to show that around two-thirds of the variation in cancer rates between organs is explained by differences in stem cell division rates, and therefore suggested that 'random' mistakes in DNA copying during stem cell division are the underlying cause of the majority of cancers⁴.

Unfortunately, the media headline that 'most cancers are bad luck' led many to announce with delight that they could keep their unhealthy habits and stop worrying. Whilst this bold headline may have had some element of evidence backing it, being based on the two-thirds figure from the study, it overlooks the quite significant one-third that ARE seemingly influenced by external factors. It also ignores the important suggestion that environmental factors might contribute to these seemingly 'random' mutations that accumulate during cell division.

In fact, another study, which analysed some of the same stem cell division data⁵, led to the second headline – 'Study suggests cancer is not 'just bad luck'². This study argued that just because a tissue with more cell division is more prone to cancer-causing mutations, it doesn't mean that these are 'random' mistakes. Environmental factors could easily contribute to mistakes made during cell division, just as they can cause mutations in non-dividing cells. The researchers used different mathematical models based on this idea, and also looked at the types of mutations found in different cancers to try and figure out what proportion look like those often caused by external factors. Their analysis, contrary to the first study, suggested that

only 10-30% of cancers are due to 'random mistakes', with the majority involving some lifestyle influence⁵.

You might ask how two rigorous scientific studies can give such different conclusions. The reality is, the maths is complex – the groups constructed different mathematical models based on slightly different assumptions and predictions in order to analyse the available data. The real answer may be somewhere between these two figures, and as we research more into the factors which promote DNA mutation and cancer growth, these models and estimates will continue to improve. But one thing is for sure – there is certainly SOME, probably fairly significant, contribution of environmental factors to our risk of developing cancer.

The take-home message is that nobody is immune to cancer. DNA mutations will happen – it is a fact of life. And sometimes, although thankfully rarely, a particularly unfortunate cocktail of mutations may arise which leads to cancer developing. There is nothing we can do that will guarantee this won't happen. However, we can certainly stack the odds in our favour and drastically reduce the frequency of these mutations and the chance that cancer will develop. Research is continually improving our understanding of which lifestyle factors contribute to cancer development, and although we are still bombarded with confusing and sometimes conflicting reports on what we should and shouldn't do, there are some very well-supported recommendations, as detailed by Cancer Research UK⁶: don't smoke, drink less alcohol, eat lots of fruit and vegetables, maintain a healthy weight and avoid excessive sun exposure. It might sound boring, but these really are some of the best things you can do to try and minimise those risky mutations! ■

References

1. Gallagher, J. (2015) <http://www.bbc.co.uk/news/health-30641833>
2. Gallagher, J. (2015) <http://www.bbc.co.uk/news/health-35111449>
3. Hanahan, D. and Weinberg, R.A. (2011) *Cell* **144**, 646-674
4. Tomasetti, C. and Vogelstein, B. (2015) *Science* **347**, 78-81
5. Wu, S., Powers, S., Zhu, W. and Hannun, Y.A. (2016) *Nature* **529**, 43-47
6. Kirby, J. (2011) <http://scienceblog.cancerresearchuk.org/2011/12/07/the-causes-of-cancer-you-can-control/>