Cancer and ageing are like two sides of the same coin

Peter Medawar: “If the effects of mutations were restricted to the later stages of life, carriers of the negative mutation would have already passed it to the next generation“.

# Part one: Age is not selected for

The generally accepted theory about cancer is that it is caused by an accumulation of mutations in different cells. When the number of mutations in a cell crosses a certain threshold, then the mutations exhibit themselves as cancer. One definition of aging itself is that aging is the increasing accumulations of changes in the genome as well as the changes in epigenetic markers. (<https://en.wikipedia.org/wiki/DNA_damage_theory_of_aging>) . Therefore in a sense, the onset of cancer with age is almost inevitable.

Given that with increasing number of cell divisions, the accumulations of genetic and epigenetic changes from the template are inevitable, there must be robust dna repair mechanisms to re-mark these changes to their original forms. While there is some evidence that in the case of epigenetic markers, there may be a case for reversing these aging effects, there is little to show that the genetic modifications that come with increasing cell division can be reversed. In fact, these genetic modifications may be passed on through the germline by the father (<http://www.nature.com/news/fathers-bequeath-more-mutations-as-they-age-1.11247>)

While we have in the last two hundred years or so, increased the average life expectancy in humans from sub 40 years to over 73 years now, there is little evidence that the lifespan itself has changed over the last 2000 years or so (<http://www.livescience.com/10569-human-lifespans-constant-2-000-years.html>). This means that while the effects of medicine has targeted diseases at younger ages through antibiotics and better infant care, there has so far been little effect on the other extreme of the spectrum. There seems to be some cell biology induced limits that we are hitting against. These may be of two types – cell degradation and telomere shortening

# Part Two: Cancer and Ageing - Telomeres

Cancer may be termed as malfunction of a cell in term of excess replication. One of the regular cell functions that stops this excessive cell division is the limited telomere expression which puts a natural limit on the number of cell divisions. This limit is what is called the Hayflicks limit. Now while this hayflicks limit helps the body stop cancerous cells from dividing without end, it also puts a limit on our natural life spans. (<http://www.nature.com/nature/journal/v448/n7155/full/nature05985.html>) This means that not just in cause (increasing number of mutations), but also in effect (telomerase increases age, but also increases cancer incidence), cancer and ageing are similar.

# Part Three: Cell degradation is not programmed

While life spans of some organisms last few hours to days, some last for hundreds of years. Humans have a highest recorded life span of 123 years. What does this mean? It means that the biology of cells itself does not impose a condition on longer life spans. Rather it is a by-product of other selections that are happening. Clearly evolution may be selecting for immortality of the gene pool (or the species) while we, as individuals, are interested in longer survival of the individual.

# Part four: Selecting for cancer

Given this lack of selection for age promoting genes, can we find genes which promote age and have some form of intervention over nature’s selection. There is evidence that we can. (<https://www.rt.com/news/318330-us-science-longevity-genes/>) So let’s say that genes fall into a few categories.

1. Genes with positive function.
2. Genes with positive function but maybe negative side effects which are not selected for (for example suffering during old age)
3. Genes with no function (or remnant of past positive function)
4. Genes with no function (or remnant of past positive function), which may have positive side effects
5. Genes with no function (or remnant of past positive function), which may have negative side effects
6. Genes with negative function which are not selected against
7. Mutations with negative functions which can be selected against

If we were to analyse the above broad bins of gene function, we can say that (vii) can be selected against by evolution. Bins (i) and (ii) are selected for by evolution. The others which evolution does not seem to touch are bin (v) and bin (vi). (http://evolution.berkeley.edu/evolibrary/article/misconcep\_04 ) These may hold the key to both cancer, ageing, and maybe even other old age diseases like alzheimers. ([geneticliteracyproject.org/](https://www.geneticliteracyproject.org/2015/10/27/longevity-is-increasing-can-we-extend-our-lifespan-one-gene-at-a-time/) ). In fact evidence shows that alzheimers is a purely human disease and therefore may have been included as a byproduct of some other factor that was selected for. Having said that, we must note that construction of these bins is very difficult. While we can design experiments to map all the relevant genes back to a function, we don’t have a mechanism yet to map all the functions, paste and present, of one gene

A potential study to carry out may be to use mouse models as the basis for knocking out one gene at a time and selecting for those genes which while leading to least number of mutations over longer number of division cycles do not alter the net mouse function as per certain parameters. This in a sense would be in a programming sense, optimizing for the ideal set of features in a case where evolution does not really work. If we look at the proteins expressed from these gene sets, we may be able to use protein inhibitors to have the same effects.

(<http://rsif.royalsocietypublishing.org/content/early/2009/03/06/rsif.2008.0520.focus>)

Thus cancer, ageing and indeed evolution itself are linked through the rubric of mutations and are two sides of the same coin.