



MY YEAR AT THE WIKO:
A YEAR OF EXPLORATION
AND WONDERFUL SURPRISES
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Adam Wilkins was born in 1945 in Columbus, Ohio, USA but grew up in New York City. He graduated from Reed College, Portland (1965) and received his Ph.D. from the University of Washington, Seattle (1969), in the field of genetics. His principal current professional interest is in evolutionary biology, but since evolution touches on everything in biology, an interest in evolution is a license for thinking about many biological subjects. He has published a moderate (not huge) number of articles, including original hypotheses, in areas ranging from bacterial physiology and bacteriophage molecular genetics to eukaryotic cell biology, eukaryotic developmental biology, and multiple subjects within evolutionary biology. His books include two advanced texts, the first in developmental genetics, the second in developmental evolutionary biology. In 1990, he became the Editor of the general biology review journal *BioEssays* and served in that capacity until 2008. Since then, he has become a wandering scholar, with his year at the Wiko (2009–10) being his second year of academic vagabondage. – Address: 12 Bramley Way, Hardwick, Cambridge, CB23 7XE, Great Britain. E-mail: wilkins316@btinternet.com

Confession may be good for the soul but it can be hard on the ego. A physical parallel would be taking cod liver oil, which is good for one's health but not a pleasant experience. Nevertheless, whatever the benefit/cost ratio of the exercise, here comes Confession no. 1: I have dithered terribly in writing my "Arbeitsbericht" and it is now two months past the initial deadline. One of the reasons is that – Confession no. 2 – I am somewhat embarrassed that there is not more tangible evidence of the fruits of my efforts. The main reason for the delay, however, is that I am still not sure exactly what is wanted. "Arbeits-

bericht” translates as “work report”, which sounds sober and serious. One infers from the term that it should be an objective, fairly complete, balanced evaluation of what was achieved, along with some preliminary evaluation of its significance. On the other hand, we are told that it should be a “personal” account, with some description of what the whole experience meant to us as sentient individuals. Putting the two things together, one gathers that, on the one hand, it should be detached, factual, objective, and complete and, on the other, subjective, perhaps even a bit light-hearted, and concentrate on the things that mattered most personally. Hmmm ...

Perhaps, I thought, one can seek guidance from past reports as to what the report should be. Alas, the styles and content of last year’s compilation vary all over the place, from the totally whimsical to the academically austere. One that particularly struck me was a meditation focussed on how difficult it was to write the Arbeitsbericht. While I suspect that kind of essay was not *quite* what the Rector and governing board had in mind with their request for a report, I was deeply sympathetic.

And then there is the subterranean question: who are the intended audience? The governing body of the Wiko – to help reassure them that they had not wasted their money on this group of Fellows?; the staff – to reassure them that they had not wasted their time or been underappreciated?; future Fellows – as either encouragement to do their best or, perhaps more importantly, as a set of cautionary tales on what not to do?; or, perhaps, even ourselves, at least in part – to help us consolidate and understand the whole remarkable experience? Probably all of the above, but since the intended readership heavily influences what you write, an article for different audiences is, inherently, a difficult proposition.

But it would be cowardly to shrink from the task just because I am not sure what is wanted, what the format should be or, indeed, who the primary target audience is. I will, therefore, stop dithering, just get on with it and hope for the best. I will start by describing the work that I intended to do and what was actually accomplished and then give a few more personal words on what the whole Wiko experience meant to me.

I came to the institute intending to write a book on the evolution of the human face. I am an evolutionary biologist who is particularly interested in the ways that animal forms and individual anatomical features have evolved over time, with my last big book being on the special genetic foundations of developmental evolutionary change. And, in this regard, the human face is a particularly interesting anatomical feature of a particularly interesting animal species (us). While all complex animals have faces, that is, concentrated

anterior areas of sensory perception (specifically the senses of vision, olfaction, taste, and hearing, if you count the outer organs of hearing as part of the face), human faces are exceptional in two properties. First, we have probably the most physically diverse set of faces of any animal species (though our nearest cousins, the Great Apes, also have highly individual, hence diverse, faces). Second, we use our faces to an unprecedented degree to communicate states of feeling and intention, often in conjunction with speech. Since no other species has true language, though several have some of the rudiments thereof, the use of our faces in connection with speech is undeniably unique and a late evolutionary development, since the Great Apes have a large facial expressional repertoire.

Now, there is a large and growing literature on facial expressions, and a great deal of popular interest in this. There is also an even bigger literature on human evolution. Yet there is, as far as I know, no serious general treatment of the evolution of the human face specifically. How did the human face evolve its special properties? What were the foundations in earlier primate evolution and how did the unique features arise? It is clear, of course, that you cannot treat the evolution of the face in isolation from that of the human head as an integrated entity or from the evolution of our species in its general features. Hence, an account of the evolution of the human face would have to be embedded within the larger context of human evolution, one that explains (or attempts to explain) the special features of the face in terms of the general evolutionary trajectory of humans over the past six million years, the point when the hominid branch split off from the Great Apes lineage. Given the centrality of the face to our social interactions, its evolution, in my opinion, is a fascinating subject and could make an excellent book for the educated and curious general reader.

But, as the word “intending” two paragraphs above indicates, things did not go quite according to my initial plans. I estimate that I spent only about a third of my working time at the Wiko on this project and in the end did very little writing for it. What I did do for this project was a lot of reading and thinking, all of which was valuable, indeed essential, for getting my thoughts in order. Two things, in particular, stand out. The first is that the current evidence indicates that the lack of a muzzle in humans (a genuine distinguishing feature from most mammals and many primates) reflects quantitative alterations in various so-called molecular “signalling pathways” that have been well characterized. The shorter the period of operation of these pathways, mostly following birth, the shorter the muzzle will be. This simple conclusion will certainly require some modification, but as a first step it has value for understanding one of the two key physical features

that distinguish our face. (The other is the verticality of our face, compared to most other mammals, which reflects our larger brains, causing a rounding of the head and a pushing forward of the neurocranium.) As far as I know, however, this explanation of muzzlelessness has not been previously elaborated in the literature. Its significance? Our lack of a muzzle plays a crucial role in what and how we eat, how we speak, and not least, how we use our faces for expression. Hence, one of the new goals of the book will be to develop this idea with molecular/genetic/developmental specifics and in a fashion that will be clear for the general reader. The second area that opened up for me – though I started with some awareness of its importance – is how much one has to think about certain aspects of brain evolution, in particular certain evolved kinds of “rewiring”, in order to account for the expressive capacities of the face. What I will try to do in this part of the book is to frame the questions about the evolution of brain regional connectivity clearly while making some tentative suggestions.

In effect, I laid the foundation for actually writing the book and I hope to do that in the year ahead, which I will do at STIAS (the Stellenbosch Institute for Advanced Study) in South Africa. But how could I neglect a subject that I find so fascinating during my time at the Wiko? The answer is simple: a second project caught hold of me and would not let me go or, more accurately, I refused to let it go because of its interest and potential significance. This involved the development of a new hypothesis on the first steps in the development of cancer cells.

This is wholly different from my first project, hence perhaps a word of explanation is needed. I spent 19 years as Editor of a very broad-ranging, general biology journal (*BioEssays*). During this time, I was not only exposed to virtually all areas of biology but, of course, also had to understand what I was being exposed to. One of the many subject areas that were, at first, new to me but which I found intensely interesting was that of cancer biology. In June, 2009, two months before coming to the Wiko, I heard a talk at a conference in Israel on some work in yeast genetics that I found fascinating and that started me thinking about how cells can radically alter the regulation of their genes under certain conditions. Further discussions and reading led me to connect the yeast findings with the biology of cancer cells. By late August, 2009, just before arriving at the Wiko, I had the germ of the idea.

That idea itself is fairly simple. It is based on the fact that there are certain “selfish” genetic elements in our genetic material, our “genome”, that are termed “retrotransposons” (RTNs). These actually comprise a very large part of the genome, about 45 %

(while long-term descendant sequences of such elements, no longer recognizable as such, might comprise another substantial fraction). A key fact is that many RTNs are induced by various forms of cellular physiological stress, ranging from various kinds of (chemical or radiation) poisoning to viral infection to senescence. When induced by such treatments, RTNs often alter the activities of contiguous genes, either activating or repressing their expression. From this fact, it is easy to construct a fairly straightforward hypothesis as to how RTN activation might be the first step in the creation of cancer cells. In particular, it would help explain how various carcinogens that do *not* induce DNA damage – a fact that is not comfortably handled by the reigning paradigm in the field (the somatic mutation theory of cancer) – might act.

Initially, I felt that it would take no more than two months to work the idea up into a hypothesis paper, at which point I would submit the article for publication and switch back to my main project. In fact, it took vastly more time to do this paper and, in the end, it went through two rounds of heavy revision after submission before being accepted. Why, one might ask, did it take so much time and work? The reason is that any statement you make about cancer has to contend, immediately, with a host of related facts and ideas, either in support or in apparent contradiction. All this literature had to be explored, absorbed, and dealt with. In the end, I produced what I think is a coherent, logically argued hypothesis paper of 4000 words on the initial step(s) in cancer cell formation. That paper was published a few weeks ago (September, 2010) and constitutes the main visible output (so far) of my time at the Wiko. (The other article written and published during my Wiko year was a short, enjoyable-to-write piece on the nature of Darwin's creativity and intelligence.)

So, what exactly is the significance of what I did during my Wiko fellowship period? Sadly, it is far too soon to tell. My book on the evolution of the human face is still in the realm of potential; it is mostly yet to be written. On the other hand, the ideas have already had some public exposure through two newspaper interviews, the second of which was published in three of the major Berlin papers, and through a television interview with Alexander Kluge. Hence, even without the book as a physical fact, the project has had some use in expanding public awareness of the interest of the human face in evolutionary terms.

And the cancer hypothesis? Well, something may be logical and coherent and even seem compelling while being completely wrong. Only time, and experimental investigation, will reveal what degree of validity the idea has. My guess is that it will account for

some percentage of cancers – there is too much supporting evidence for it to be totally wrong, in my view – but the question is what percentage? If, say, it is 1–2 %, it will be at most an interesting curiosity, a sideshow to the main story of cancer. If, however, it pertains to say 30–50 % of all cancers, it will be important. And if the figure is 80–90 % or more, it will be very important, to the point of revolutionizing how we think about the disease. But, I repeat, it is too soon to tell. Even if it proves to be totally false, however – that RTN induction has nothing to do with cancer – against my intuition, the hypothesis will still have value if it stimulates a line of experimentation. Any results from such experiments would be bound to be informative. Indeed, incorrect hypotheses are often extremely valuable.

So much for the *Arbeit* side of my Bericht. Beyond the satisfaction and excitement of exploring two intriguing subjects that the Wiko year greatly facilitated, what about the human and personal side of my Wiko experience? Briefly, it was superb. If I had to characterize it as a whole, I would say that it was a year of wonderful, pleasurable surprises. First, while I certainly had looked forward to the year and expected to enjoy it, the reality exceeded all expectations. This was due, in part, to the sheer interest of the variety of different projects and the diverse set of personalities amongst the Fellows. Of course, the very structure of the activities, in particular the regular meals in which we all participated and the Colloquia, guarantee a high level of exposure to the diverse ideas that occupy the Fellows, while all sorts of interesting unexpected things invariably come into conversations. It would be an unusual meal where one had not been exposed to something new and interesting. But, equally, I would credit the staff with what makes the Wiko a special place. The staff are not only super-efficient in helping the Fellows, they also do so with warmth, friendliness, and, often, a very nice sense of humour. This was all above and beyond the call of duty. The Wiko, as a result, is a great institution without feeling at all “institutional” in the usual way.

Another surprise: how much I enjoyed learning German even as I struggled with it. This included real pleasure in just listening to the language. While I had grown up hearing my mother’s mellifluous Viennese-accented German in conversation with her sister (sadly, she never tried to teach the language to her sons), my feeling about “real” German had been shaped by exposure to too many WWII movies. As I discovered this year, the real language is actually beautiful in its tonal quality. In my post-Wiko life, I continue to study and struggle with German, but the sense of enjoyment remains. I feel deeply in-

debted to my two teachers at the Wiko, both of whom patiently endured my inadequate efforts but never failed to instruct and encourage.

A small surprise: that there was the office of Fellows' Spokesperson, with a man and a woman chosen to play this role. The job is that of a sort of shop steward, someone to handle any grievances of the Fellows by dealing with the "management". Why, I wondered, would a place as wonderful as the Wiko need someone to mediate with the institution itself? What sort of problems might require this? Well, my surprise increased when I was elected the male Fellows' Spokesperson and soon discovered that there were indeed some problems, where some mediation was needed. I did not enjoy all of this work but, for the most part, it was rather fun, helping to sort out various matters. It helped give me the feeling of contributing, in a small way, to the Wiko beyond the academic side.

Then there were the multiple surprising pleasures of discovering Berlin: the excellent (and relatively inexpensive) restaurants, the music scene (both the Philharmonie and some great jazz clubs), the art scene, the zoo, the museums, and, not least, the interesting and pleasurable simple experience of walking around different parts of the city, getting a feel for the character and history of the place. Again, I had expected to enjoy this side of things; it was just that the reality was even better than my rather pale prior imaginings. Of course, it might be said that the pleasures of Berlin are totally ancillary to and unrelated to the Wiko *per se*. But I am not so sure: somehow the city both complemented and enhanced the direct pleasures of being at the Wiko. Particularly because I was studying German, excursions into Berlin felt like a continuation of the marvellous learning experience that my year at the Wiko proved to be.

One could go on but the above is probably sufficient to convey the feeling of the experience. Briefly, I had a truly exceptional year and I am, and will always remain, deeply grateful to the staff, my fellow Fellows, and Berlin itself, for making it so.