Epilogue

Résumé and Visions: From CMV Today to CMV Tomorrow

Ulrich H. Koszinowski

This new book on cytomegalovirus is both a timely update and an extension of the previous book, now giving more room also to clinical observations and studies. '… and what is the use of a book,' thought Alice, 'without pictures or conversation?' (Lewis Carroll, *Alice's Adventures in Wonderland*). This book is written by a selected trustworthy group of world-renowned virologists …and, yes, it has great pictures!

It is the inevitable fate of all published scientific observations from a given period to be digested and to end up as a state-of-the-art review book. The digest is made for us by other experts and we are usually more than happy to trust their work. The book gives us the advantage to memorize less than we used to or had to. We can just look it up. Such a collection of reviews must be counted, according to Orwell's definition, among the best books: '…those that tell you what you know already'.

I have the additional pleasure to know almost all authors as personalities and not only from their writings. Science is made by humans. It provides pleasure to hear the familiar sound which adds another dimension to their writing. Thus, for me it is not only written but almost spoken text. As anybody else I have colleagues that I favour more than others. How can I control that my trust is not too much controlled by sympathy? Thus, knowing the authors may not be of advantage in all cases. This brings me to the quote of Terentianus Maurus 'pro captu lectoris, habent sua fata libelli' meaning that books have their destinies according to the capacity of the reader. Each of us will take from this attractive thesaurus what she or he is able to. So many presents are laid out and we have many options and choices, indeed.

Such science books in review form often deal with matters we are already pondering, areas we wish to venture in order to ask new questions or we are even working on. Because the answer we gave to a scientific question yesterday may be quite different from the answer to the same questions asked today or in the future such a book must have a limited half-life. Answers offered suffer from systematic oversimplification: a hallmark of science. Already a major oversimplification is what we believe to constitute the properties and functions of a cytomegalovirus protein. We constantly find new functions for old candidates. In addition, some of us have this itch to coin new names whenever describing a new function for a protein of an already known function. But what do we really know for safe about gene functions and how many of such renaming events lie ahead of us until we know? This protein-name-function connection bears difficulties. If we constantly name and rename any of these translation products according to functions we describe to them, even when the observation has not yet been reproduced, we duplicate the maze already presented by CMV as we know it today. Abraham Lincoln said 'How many legs does a dog have if you call the tail a leg? Four. Calling a tail a leg doesn't make it a leg.'

No particular vision is needed to predict that there is serious work coming up. The CMV of today is not the CMV of tomorrow. What will be the state of the gene–protein–function connection in the future? Good enough that this book considers research only until end of 2011. At the recent 2012 Herpesvirus Workshop it was reported that ribosomal footprinting reveals an unexpected complexity of translation products coming from individual ORFs. This demonstrates the value of measuring gene expression at the level of translation. The abundance of footprint fragments in deep sequencing data reports on variability and amount of translation of a gene. In addition, footprints reveal the exact translated regions. This apparently more than doubles the number of CMV proteins known today. How will we confirm this complexity and annotate functions of these translation products?

This problem is not easy to solve. After all, what is THE human cytomegalovirus (HCMV)? Known isolates vary considerably and isolates do not describe a clonal entity but an inhomogeneous group of genomes that, taken together, make a phenotype. In addition, the lack of clonal stability and the difficulty to propagate some of the strains will make it very difficult to study certain CMV strain properties. Only from the genetic side there is hope coming through sequencing and systems biology approaches.

With regard to functional properties of individual translation products there is no easy solution. Genetic engineering for studying specific functions will necessarily get more complex. A more stumbling problem may pose the ignorance-hierarchy in CMV research. We live in an anthropocentric world. Clearly, only HCMV is the relevant pathogen, the subject is funded best, and HCMV research is published, often ignoring work on CMVs from other species. Rhesus CMV is next in line and needs to consider only HCMV research. Then follow the rest, guinea pig CMV, rat CMV and mouse CMV at the end of the 'relevance chain'. This ignorance is justified to some extent: there is high genetic variability already among human CMVs with respect to gene sequences, gene numbers and gene functions. Positional identity is clearly not identity and similarity is just what it is. Yet, this ignorance is not fruitful. Given the flood of data coming up it is perhaps more fruitful to use Occam's razor (entities must not be multiplied beyond necessity), to assume comparable gene functions unless a divergence is clearly proven. Namely, without proposals on potential functions of newly identified proteins by work on animal CMVs there is little hope to unravel the complexity of new HCMV gene products. Work on animal CMVs cannot give right answers for HCMV, yet it can ask right questions.