Laudatio for
Professors S C Harrison, Harvard University and
M G Rossman, Purdue University,
Recipients of the Year 2001 Paul Ehrlich- and Ludwig Darmstaedter Prize
for their pioneering contributions to
determination of the complex shell of spherical viruses

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About 2400 years ago there was an olive grove outside Athens called Hekademia after a fellow greek. This grove was made available to Plato and his pupils, who came to form the first academy. Above the entrance of this academy there was a sign which read "Let no one enter who is ignorant of geometry". The greek scholars were highly impressed by three-dimensional symmetrical structures and equalled four of them the tetraeder, the cube, the octaeder and the icosaeder with the presumed basic components of nature – air, water, earth and fire. The remaining platonic body, the dodecaeder, represented what remained, the quintessence.

What has all this to do with the 2001 Paul Ehrlich and Ludwig Darmstaedter Prize? Both Prize recipients, Dr Stephen C Harrison and Dr Michael G Rossman, are x-ray crystallographers, and scientists with such an orientation can only go about their work if they have crystals to examine. Crystals represent symmetrical aggregates of identical structures. Already in the 1930s it was found that virus particles from plants could form crystals. The observation of such crystals rendered Wendell Stanley from USA a Nobel Prize in Chemistry in 1946. Their identification also stirred a discussion of whether viruses represented dead or live material. Such a discussion does not appear meaningful today but it highlights the phenomenon that there are two distinct phases in the life cycle of viruses. One phase are the parasitic events inside infected cells which lead to production of a large number – hundreds of thousands or millions – of new particles that can spread the infection. The other phase is the virus particles themselves, which represent essentially passive transport vehicles. It is sometimes said that virus particles are a package of bad news. If we can find chemical or immunological means of blocking the capacity of virus particles to infect cells we can prevent or curtail infections. The fundamental discoveries of this years prize recipients have provided new opportunities for such interventions. But before I comment on these new opportunities let me return to the original discoveries.

Why is it that the large virus particles can form crystals? The reason is that the genetic material which in essence carries the infectious property of a virus needs a protective shell during its transport between cells. In order to save information this shell is built up of identical subunits. These subunits most often form a spherical structure exploiting the most complex of the platonic bodies, the icosahedron. Because of this highly symmetrical built-up billions of particles that by themselves can only be seen with the electron microscope can form crystalline structures which we can see with the naked eye.

The plant virus crystals, which were readily produced, represented an obvious tantalizing challenge to crystallographers. But compared to the crystal structures resolved in the 1960s, the childhood of crystallography, they appeared overwhelmingly large and complex. New techniques had to be developed to orient the crystals and to distinguish from the myriad of x-ray spots on a film a repeated occurrence of unit structures. The prize recipients of this year managed to develop techniques to handle the daunting problems of resolution of complexity.

Progressively the development of new irradiation sources that did not harm the crystals – originally they just evaporated – and also new computer systems allowing the accumulation and handling of vast amounts of data facilitated the analyses.

The break-through publications came in 1978 when Professor Harrison and collaborators could describe the three-dimensional structure of the shell of tomato bushy stunt virus and in 1979 when Professor Rossman and collaborators could provide an equally valuable information on southern bean mosaic virus. A new era started and since then we have learnt to know the three-dimensional structure of the surface components of many important spherical viruses not only of plant origin but also those causing diseases in man and in animals.

Why is it important to understand the three-dimensional structure of building stones in viruses? The reason is of course that without knowing their structure we can never fully understand their function. We live today in a fantastic, explosive phase of development of biology. Because we can now read the information in genes with a high proficiency we can accumulate a vast amount of information on the so called primary structure of proteins, the sequence of "pearls" in this one-dimensional stringed structure. But we want to understand the folding, the three-dimensional structure. Hence we move today from genomics to proteomics. Still it is not enough to understand the structure of individual components. We need also to comprehend how proteins interact, how they can form complex functional structures. This was first seen in viral shells and the discoveries made by Professors Harrison and Rossman have led to means of interpreting protein-protein interactions.

As was already alluded to, the findings they have made have opened up new possibilities to develop vaccines with a high precision of action and anti-viral compounds that block replication of such infectious agents. The anti-virals potentially can have many modes of action, blocking the docking of virus particles to cells, preventing the release of the nuclei acid from infecting particles, interfering with the function of viral enzymes etc. However I believe that no one is better equipped than the prize recipients themselves to describe how they could make the critical break-throughs and how the seminal findings they have made have opened new possibilities for applications. Thus I leave it to them to give such a presentation.

So let me end by congratulating Professors Stephen C Harrison and Michael G Rossman for their impressive achievements. The 2001 Paul Ehrlich- and Ludwig Darmstaedter Prize is only a small token of appreciation from the scientific community. Finally I wish both of you success in the work still to come.