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LETTERS TO THE EDITOR

Antigenic Specificity of Virus Structural Components

The antigenic properties of viruses are of considerable fundamental and practical interest in virology. A detailed knowledge of the structure-antigen relationship would greatly enhance our understanding of virus host interactions. It would also be helpful for the selection of suitable virus antigens for vaccine development. This communication is a theoretical approach to the problem, an attempt to relate virus structural components to their respective antigenic specificities. A recently developed theoretical approach in molecular biology, *derivation theory*, has enabled the derivation of the evolutionary sequence of virus structural components (Kilkson, 1964*a*, *b*, 1965*a*,*b*). In Fig. 1 is given a schematic diagram, derivation tree (Kilkson, 1964*b*, 1965*a*), of the structural evolution of viruses. The evolutionary derivation starts from one molecule of single-stranded nucleic acid and proceeds toward the more complex structures by additions of other structural components. The subunits of these structural parts can be expected to carry antigenic components. Since each evolutionary step may occur a number of times independently, the structural subunit diversity increases as one proceeds along the evolutionary derivation tree. The structural evolution and the increase in subunit variety should be paralleled by an increase in antigenic variety. Therefore, the more recently added structural components (Fig. 1) should be the sites of higher antigenic specificity than the structural components corresponding to the earlier evolutionary steps. The earlier evolutionary component may undergo mutations, but these are restricted by the structural bonds already in existence.

Therefore, given a virus structure, it is possible to predict the antigenic specificities of the structural components on the basis of the evolutionary derivation tree, Fig. 1. Inversely, given the antigenic pattern of a group of antigenically related viruses, it is possible to limit, and in favorable cases to predict the structures of the viruses. Furthermore, the symmetry considerations (Kilkson, 1964*a*, 1965*a*) restrict the relative numbers of different structural subunits in the virus, therefore also the relative numbers of the respective antigens.

Less rigidly ordered structural components have fewer constraints on the possible viable structural mutations. This may perhaps be a contributing

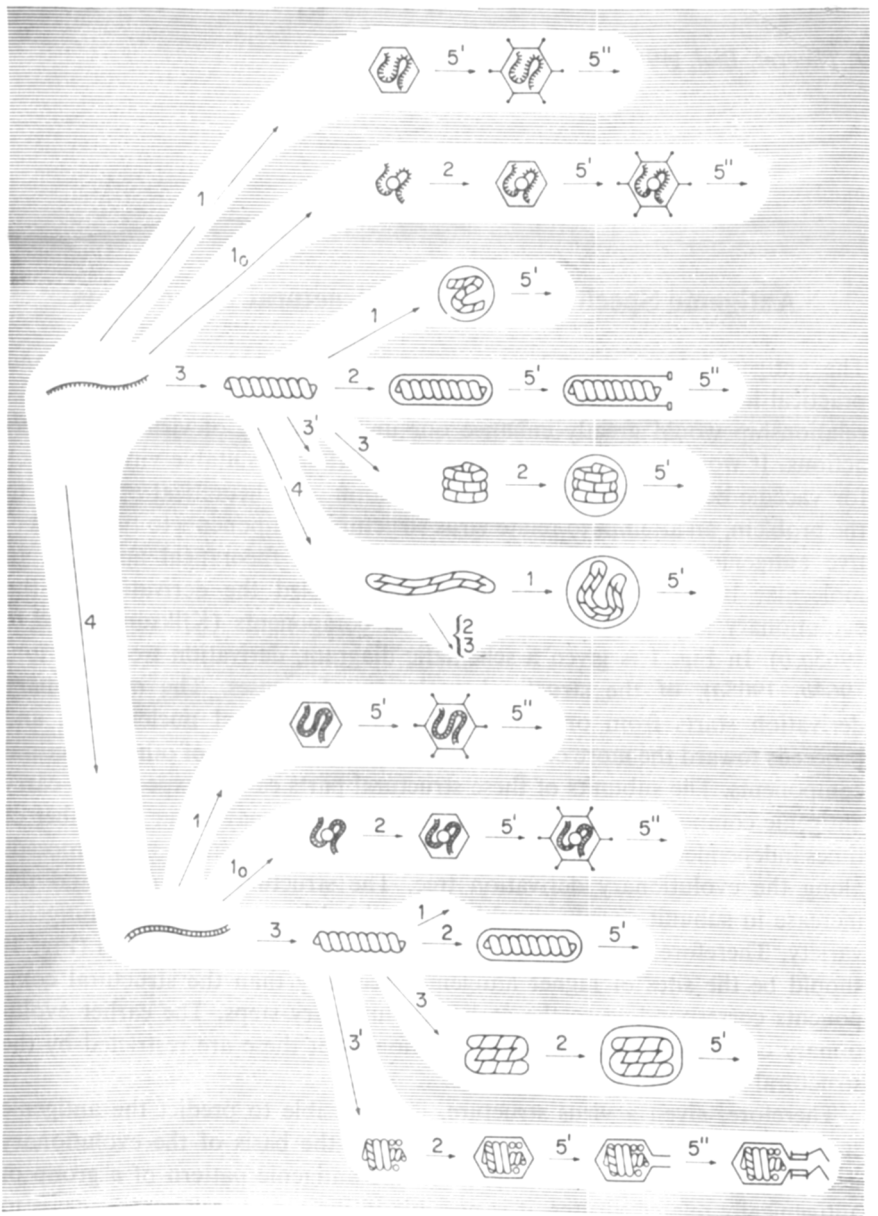

FIG. 1. Derivation tree of the structural evolution of viruses. The evolution proceeds from left to right. The arrows signify major evolutionary steps, the numbers refer to the analytical derivation processes (Kilkson, 1964*b*, 1965*a*). The antigenic specificity of the structural components increases from left to right, the latest additions (far right) having the highest specificities. Some of the intermediate evolutionary structures are unlikely to exist as viruses, due to their lack of stability (Kilkson, 1965*a*). Haemagglutinin can be expected on the outer components of the viruses, particularly in association with 5′ additions. Adenovirus 5 (see in text) corresponds to arrow sequence 415′, though the possibility of 41_0 25′ cannot be completely ruled out. The two structures would differ only in a special nucleation center (process 1_0), this could also add another rather non-specific antigen. So far there are no observations to support the existence of such a component in adenovirus 5.

factor to the frequent antigenic mutations in myxoviruses, these have rather loosely organized outer coats (Horne & Wildy, 1963).

Of special fundamental interest could be various phage tail structures (phage tail derivation tree, Kilkson, 1965*b*). Because of the large number of specialized structural parts the respective subunits should present an excellent system for genetic-evolutionary studies.

The evolutionary derivation tree (Fig. 1) predicts that the most recent structural additions, and therefore the most specific antigens, are to be expected on the outermost and exposed structural parts. A chemical treatment is likely to destroy these components. This suggests that chemical inactivation of viruses may not be a good approach for the production of specific antigen, since the outer components of the virus are most likely to be denatured by the treatment. A preferable approach would be selective removal of the virus nucleic acid. A favorable method for isolating highly specific antigens would be a combination of depolymerizing the virus and digesting the nucleic acid enzymatically, if the depolymerization could be performed without denaturing the structural subunits. Non-structural antigens have to be obtained from infected cell.

Good structural and antigenic data are available for adenovirus 5 (Valentine & Pereira, 1965). The evolutionary derivation tree (Fig. 1) predicts the following structural evolutionary sequence for this virus: coat protein, a specialization of vertex subunits, attachment of spikes, formation of globular tips of the spikes. According to the theory presented in this communcation, the antigenic specificities of the subunits of these structural parts should increase in the same order. This predicts the following specificities to adenovirus 5 antigens: α-group specific; β-subgroup specific; δ-subgroup specific or higher specificity (the morphological site of δ is not known more exactly); γ-type specific. The experimentally observed antigenic specificities (Valentine & Pereira, 1965) agree well with these theoretical predictions.

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