Adenoviruses Types 20, 25 and 28: Atypical Members of Group II

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Rosen (1960) divided human adenoviruses into three groups with differing haemagglutinating properties, and a fourth group comprising types without haemagglutinating activity (Table 1). At that time, types 20, 25 and 28 had not yet been discovered. These types were later incorporated into group I, since they exhibited no haemagglutinating activity with rat blood cells, while showing some haemagglutinating activity with monkey blood cells. It will be shown that these virus types closely resemble viruses of group II, except that they do not haemagglutinate rat blood cells. On the other hand, there is no single criterion warranting their classification in group I.

Table 1. Classification of human adenoviruses

<table>
<thead>
<tr>
<th>Types</th>
<th>Haemagglutinating activity</th>
<th>Group (Rosen, 1960)</th>
<th>Group (Huebner, 1967)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3, 4*, 7, 11, 14, 16, 21</td>
<td>Monkey blood cells</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>20, 25, 28</td>
<td>Monkey blood cells (weakly)</td>
<td>?</td>
<td>D†</td>
</tr>
<tr>
<td>8, 9, 10, 13, 15, 17, 19, 22, 23, 24, 26, 27, 29, 30</td>
<td>Rat blood cells</td>
<td>II</td>
<td>D†</td>
</tr>
<tr>
<td>1, 2, 4*, 5, 6</td>
<td>Monkey blood cells (weakly)</td>
<td>Some types:</td>
<td></td>
</tr>
<tr>
<td>12, 18, 31</td>
<td>Rat blood cells‡</td>
<td>III</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>None§</td>
<td>IV</td>
<td>A</td>
</tr>
</tbody>
</table>

* Type 4: intermediate between groups I and III (Norrby & Wadell, 1967).
† McAllister et al. (1969).
‡ Incomplete haemagglutination pattern.
§ Type 12 shows haemagglutinating activity with rat blood cells (Bauer & Wigand, 1963; Schmidt, King & Lennette, 1965).

Prototype strains of type 20 (931), 25 (B.P. 1) and 28 (B.P. 5) were obtained from Dr Wallace P. Rowe, Bethesda. Three wild strains of type 25 (201089, 201090 and 201091) and one of type 28 (96012) were provided by Dr Leon Rosen, Honolulu, one further strain of type 25 (Karachi 4) by Dr Wade P. Parks, Houston. Three further strains (B 746, 826, T 5-4027), related to type 20 in neutralization, but to other types in haemagglutination-inhibition (Wigand & Fliedner, 1968), were provided by Drs W. Belian, Berlin, and E. H. Lennette, Berkeley, respectively. They are referred to as ‘intermediate type 20 strains’. All viruses were propagated in HeLa cell cultures.

Biological properties

Haemagglutination with rat blood cells. As found by others (Bell, Rota & McComb, 1960; Rosen, Baron & Bell, 1961), the virus strains mentioned above did not haemagglutinate rat blood cells at temperatures of 4°, 20° and 37° with the exception of the three intermediate type 20 strains, which readily agglutinated rat blood cells. It is noteworthy, that at least one strain of group II (type 19, strain RAMIREZ, submitted by Dr E. H. Lennette) failed to agglutinate rat blood cells despite a fairly high infectivity titre.

Haemagglutination with monkey blood cells. Haemagglutinating material was obtained with difficulty and in moderate titre. Centrifugation experiments showed that complete and incomplete virus particles exhibited haemagglutinating activity, whereas—at least
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for types 20 and 25—no 'soluble' haemagglutinin was found. This is in accordance with the behaviour of haemagglutinins for monkey blood cells, which are demonstrable in low titre in some types of group II (Wigand & Stöhr, 1965). In contrast, all virus types of group I possess a soluble haemagglutinin (Stöhr & Wigand, 1965).

Cytopathic effect and cytopathology. As shown earlier (Wigand & Bauer, 1964), two characteristic kinds of adenovirus CPE can be distinguished in HeLa cell cultures: retraction type CPE shown by all group I and III viruses with the exception of type 4, and rounded-cell type CPE shown by all group II viruses except type 8. Types 20, 25 and 28 resemble group II viruses in producing rounded-cell type CPE; the cellular lesions observed in stained preparations were also identical (Loytved & Wigand, 1969).

Oncogenicity. This property does not appear suitable for the discrimination of adenovirus subgroups any more, since the number of virus types inducing tumours in hamsters—either directly or after cell transformation in vitro—is steadily increasing.

Pathogenicity for man. Types 20, 25 and 28 were rarely isolated from man; at present no statement can be made on their pathogenic significance. On the other hand, types 3, 7, 14 and 21 of group I are known as types of relatively high pathogenicity, frequently causing epidemic outbreaks.

Serological properties

While many of the human adenovirus types react type-specifically, when tested in neutralization and haemagglutination-inhibition tests, there are intricate serological relationships, which are virtually confined to virus types within the group. Only a part of them is evident by cross-testing with animal immune sera (Stevens et al. 1967, Wigand & Fliedner, 1968); some may only be demonstrated in human infections (Kasel et al. 1965). Viruses of group I show some cross-reactions in neutralization and in other tests (Wigand et al. 1965, Stevens et al. 1967). There is, however, no single instance reported of a cross-reaction of types 20, 25 and 28 with any member of group I. On the other hand, the strong reciprocal cross-neutralization between types 25 and 15 is well-known (Rosen et al. 1961). Type 28 antisera exhibit haemagglutination-inhibition with type 27 antigen (Wigand, 1968).

As to type 20, three intermediate virus strains haemagglutinating rat blood cells have been found, closely related to type 20 in neutralization. One of them (T-4027) is related to type 13 in haemagglutination-inhibition, the other two have a haemagglutinating moiety of a new type 34 (Wigand & Fliedner, 1968).

No cross-reaction of group I hamster tumour sera with tissue culture antigens of types 20, 25 and 28 or of group II viruses were observed in complement fixation, while most members of group I crossed with one another (Huebner, 1967). Recently McAllister et al. (1969) observed a common T-antigen shared by all members of group II and also by types 20, 25 and 28. This was demonstrated by complement fixation with sera from hamsters bearing tumours induced by cells transformed by adenovirus 19 and 26.

Structure and biochemical properties

The structure of types 20, 25 and 28 virus particles and of their soluble components has not been investigated. Thus the length of fibres or projections, used by Norrby (1968a) as a criterion for classification, is at present unknown. These types apparently do not form a dodeca as a morphological substrate for the soluble complete haemagglutinin, which was found for most types of group I (Norrby, 1966, 1968a) and all types investigated of group II (Gelderblom et al. 1967, Norrby, 1968b). If this structural component should be present in types 20, 25 and 28, but inactive against rat as well as monkey blood cells, this at any rate would not serve to distinguish between the two groups.
In chromatography on DEAE columns, infectious virus and hexon of types 20, 25 and 28 exhibited an elution pattern similar to viruses of group II (unpublished observations; c.f. Gelderblom, Wigand & Bauer, 1965).

An analysis of the DNA base ratios of purified adenoviruses of types 1 to 28 (Piña & Green, 1965) showed, that types 20, 25 and 28 fall into the category with a high (G+C): (A+T) ratio, as do all viruses of groups II and III, while all types of group I exhibit a lower G+C content.

Conclusions

It is suggested that workers in the adenovirus field should use Rosen’s group designation (I to IV) rather than that of Huebner (1967) (A to D), which is based on the relationship of T-antigens within the group, since the two classifications correspond to each other (Table 1) and Rosen’s proposal has the priority. As to types 20, 25 and 28, only the failure to agglutinate rat blood cells distinguishes them from the other group II viruses, whereas they differ from group I viruses in haemagglutinin properties, cytopathology, serologic relationship of virion and T-antigens and biochemical findings. In all of these properties types 20, 25 and 28 resemble group II viruses.

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REFERENCES


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