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Some comments on the importance of myxoviral glycoproteins

ENRIQUE VILLAR and JOSÉ A. CABEZAS*
Departamento de Bioquímica y Biología Molecular, Facultad de Biología, Universidad de Salamanca, Plaza de la Merced 1-5, 37008 Salamanca, Spain

The interesting comments of Schulze and Manger [1] on the importance of glycosylation of Influenza Virus (an Orthomyxovirus) outer membrane glycoproteins for the generation of viral diversity are right. However, in our opinion, this is just a part of the whole picture and it should be pointed out that viral envelope glycoproteins could also be important in some steps of the viral infection cycle. In fact, we have found [2] that in a Paramyxovirus as Newcastle Disease Virus (NDV) the envelope glycoprotein HN, with hemagglutinin and neuraminidase (=sialidase) activities, interacts with the inner non-glycosylated matrix protein, the M protein, and such interactions could play an important role *in vivo* in the budding of the virus from the host cell.

Furthermore, it has been previously shown: (i) that segments of the glycoproteins of Sendai Virus (another Paramyxovirus) are exposed on the cytoplasmatic surface of the host plasma membrane [4], (ii) that the M protein interacts with the ribonucleocapsid [5–7], and (iii) that the interactions between the M protein and the ribonucleocapsid are required for virus assembly [8]. With such a picture in mind we studied the possible interactions between the HN and M proteins in NDV, and we have found that these interactions are electrostatic in nature [2]. Thus, the interaction between the HN external glycoprotein and the internal matrix non-glycosylated M protein may be important *in vivo* as a part of the viral budding mechanism from the host cell. The M protein, already bound to the ribonucleocapsid, does recognize the citoplasmatic segment of the HN glycoprotein, and the interaction between them may be one of the events for triggering viral budding.

In Schulze and Manger article [1], it is clear that envelope glycoproteins are also involved in the generation of viral diversity, but it is also evident, from the above mentioned and other articles, that viral glycoproteins play important roles in the viral cycle, even through their non-glycosylated part, and that interactions between glycoproteins and non-glycosylated internal proteins are also essential for the viral survival.

It should also be pointed out that in viruses with neuraminidase (=sialidase) [9] activity, like Orthomyxoviruses (influenza viruses A and B), and some Paramixoviruses like NDV and Sendai, the glycoprotein responsible of the sialidase activity also plays a key role in the viral cycle eliminating the sialic acid residue from the envelope glycoproteins, thus avoiding viral agglutination and facilitating viral spread within the host [10]. Besides, *O*-acetylesterase from influenza virus C [11], which releases the *O*-acetyl group from *N*-acetyl-9-*O*-acetylneuraminic acid and other *O*-acetyl-containing compounds [12], increases the influenza A virus sialidase activity [13]. Thus, both the release of *N*-acetylneuraminic acid by sialidase from influenza viruses A and B and the release of the *O*-acetyl group from *N*-acetyl-9-*O*-acetylneuraminic acid by *O*-acetylesterase of influenza virus C may be considered as mechanisms for better succeeding in infection, by modifying the carbohydrate moiety of viral envelope glycoproteins.

Although some aspects on the structure and function of viral envelope glycoproteins are now well established, much still remains to be learned about these aspects, providing many interesting challenges in this area of research. Viral glycoproteins are thus gaining great notoriety.

References

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