

Propositions belonging to the thesis:

Lysosomal neuraminidase

A unique member of the sialidase superfamily

1. Lysosomal neuraminidase is more closely related to bacterial sialidases than to the other mammalian cytosolic and plasma membrane-associated neuraminidases.

this thesis

2. The presumed membrane association of lysosomal neuraminidase is based on a misinterpretation of the results obtained with sub-cellular fractionation studies that does not take into account a possible co-fractionation of insoluble enzyme with the membrane-containing fraction.

this thesis

3. Sialidosis patients with no detectable mutations in the neuraminidase gene should be analyzed for mutations in the PPCA gene that would prevent the binding of PPCA to neuraminidase.

4. The fact that Asp-boxes are present in all neuraminidases, except in viral sialidases, contradicts the theory that Asp-boxes are required for either the beta-propeller-fold or the secretion of the enzymes.

Crennel et al. (1993) PNAS 90: 9852-9856; Roggentin et al. (1993) Mol Micr Biol 9: 915-921; Gaskell et al. (1995) Structure 3: 1197-1205

5. The existence of a group of catalytically inactive 'sialidases' in *Trypanosoma cruzi* that differ from the active enzymes by a single tyrosine to histidine mutation suggests an additional function for this group of proteins.

Cremona et al. (1995) Gene 160: 123-128

6. Breaking the barrier of the speed of light with a factor of 310 reported by Wang *et al.* serves as a reminder that even scientific dogmas can be the product of inadequate experimental approach.

Wang et al. (2000) Nature 406: 277-279

7. The observation by Bradford *et al.* that the 'immunoglobulin heavy chain-binding protein' (BiP) binds to an active site mutant of lysosomal N-acetylgalactosamine-4-sulphatase, does not imply that BiP has a role in the ER-quality control of this enzyme under physiological conditions.

Bradford et al. (1999) Biochem J 341: 293-201; Hellman et al. (1999) J Cell Biol 144: 21-30

8. The expanding family of ubiquitin-related proteins that are linked to the ubiquitin-proteasome degradation pathway, suggests that intricate regulation of protein breakdown is equally important for the maintenance of cellular homeostasis as fine tuning of protein synthesis.

Jentsch et al. (2000) Trends in Cell Biol 10: 335-342; Luders et al (2000) J Biol Chem 275: 4613-4617; Kaye et al. (2000) FEBS lett 467: 348-355; Funakoshi et al. (1999) EMBO J 18: 5009-5018; Moynihan et al. (1999) J Biol Chem 274: 30963-30968

9. The completion of the human genome project is more likely to quickly boost the value of biotech stocks than that it will result in the rapid development of a cure for the major human diseases.

<http://www.ncbi.nlm.nih.gov/genome/seq/>; Hayden, Newsweek (2000) 136: 51; Marshall, Science (2000) 288: 2294-2295; See the numerous editorials this year in scientific journals

10. To prove a fact statistical differences are often used as scientific evidence, whereas they should merely initiate research to explain the underlying causes of such differences.

11. The law of physics dictates that, regardless of the type of diet, the intake of more calories than one can burn, will result in a gain of weight.