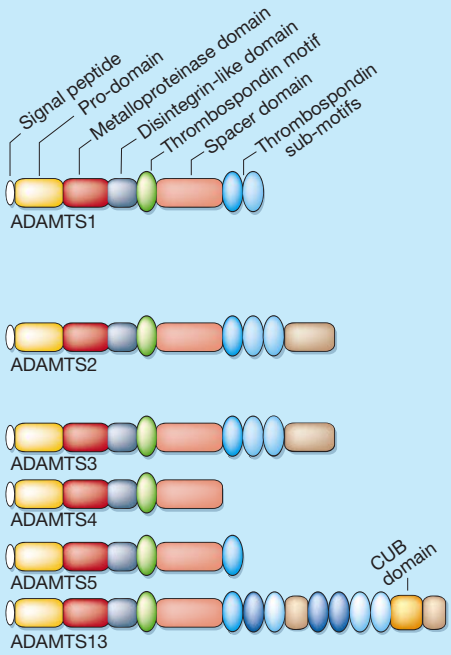

Human or animal disease caused by mutation	Deregulated expression of the protein is associated with:
Decreased growth, female infertility, ureteral, adrenal and adipose tissue abnormalities in gene-knockout mice	Wasting in cancer patients, inhibition of blood-vessel development, inflammation, ovulation, bone metabolism, liver cirrhosis
Ehlers–Danlos type VIIC in humans. Dermatosporaxis in cattle. Fragile skin and male infertility in transgenic mice	Fragile skin, maturation of spermatogonia
———	———
———	Arthritis, brain tumours, Alzheimer's disease
———	Arthritis
Thrombotic thrombocytopenic purpura in humans	Renal and neurological dysfunction, anaemia, fever, low platelet count

Figure 1 **The ADAMTS family of proteins. All the ADAMTS enzymes described so far contain a 'signal peptide', which directs them to the cellular secretory apparatus. The pro-domain is cleaved off to produce the functional enzyme; the metalloproteinase domain contains the active site; and the function of the disintegrin-like domain is unknown. This family is distinguished from a similar group, the ADAM family, by the presence of thrombospondin type I motifs (regions first identified in the platelet protein thrombospondin). The spacer domain has both cysteine-rich regions and domains that lack cysteines. The thrombospondin submotifs show limited similarity to the thrombospondin type I repeat. Some of the enzymes also have unique domains that are unlike other protein modules. ADAMTS13 is the only member of the ADAMTS family to have a CUB domain — a feature of many extracellular proteins. ADAMTS 6, 7, 8 and 9 are orphan enzymes with no known substrates, and ADAMTS 10, 11 and 12 have been identified but not yet published.**

the proper processing of type I collagen, leading to extremely fragile skin (Ehlers–Danlos syndrome type VIIC in humans and dermatosporaxis in cattle)[10]. Many of the other enzymes are 'orphans' with no known substrates.

Levy *et al.*[1] have shown that mutations in *ADAMTS13* cause the inherited form of TTP. But the exact mechanism is not so clear, and the authors suggest several possibilities. The most likely scenario is that the persistence of high levels of large VWF multimers in the blood directly causes the disease. But it could be that the lack of fragmented products is important, or even that ADAMTS13 has other substrates in other tissues.

What is clear, though, is that new treatments for patients with TTP can now be developed. At the moment, therapy involves plasma exchange to replenish the active proteinase, remove multimeric VWF, and deplete any of the circulating ADAMTS13-specific antibody. Because the proteinase activity has a long half-life, of two to three days, this is an effective treatment[11]. But now specific enzyme-replacement therapy becomes a viable alternative, especially given that as little as 5% of normal enzymatic activity may be sufficient to degrade large VWF multimers[12]. Finally, because the exact location of the *ADAMTS13* gene within the human genome has been mapped, gene therapy — along the lines being explored for treating haemophiliacs — may be a realistic option in the future for patients with inherited TTP. ■

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1. Levy, G. G. *et al. Nature* **413,** 488–494 (2001).
2. Moschcowitz, E. *Proc. NY Pathol. Soc.* **24,** 21–24 (1924).
3. Furlan, M. *et al. New Engl. J. Med.* **339,** 1578–1584 (1998).
4. Tsai, H. M. & Lian, E. C. *New Engl. J. Med.* **339,** 1585–1594 (1998).
5. Tsai, H. M. *Blood* **87,** 4235–4244 (1996).
6. Furlan, M., Robles, R. & Lamie, B. *Blood* **87,** 4223–4234 (1996).
7. Gerritsen, H. E., Robles, R., Lammle, B. & Furlan, M. *Blood* **98,** 1654–1661 (2001).
8. Fujikawa, K., Suzuki, H., McMullen, B. & Chung, D. *Blood* **98,** 1662–1666 (2001).
9. Kuno, K. *et al. J. Biol. Chem.* **272,** 556–562 (1997).
10. Colige, A. *et al. Am. J. Hum. Genet.* **65,** 308–317 (1999).
11. Furlan, M., Robles, R., Morselli, B., Sandoz, P. & Lammle, B. *Thromb. Haemost.* **81,** 8–13 (1999).
12. Barbot, J. *et al. Br. J. Haematol.* **113,** 649–651 (2001).

Daedalus

Learning from melting

The most informative chemical test of all is simple heating; just warming the sample up and seeing what happens. Some substances, such as naphthalene, melt cleanly to a clear liquid; others, such as sucrose, give a hopeless mess confusing a change of phase with molecular alteration. Daedalus reckons that a shrewd chemist learns more about a material from a melting test than any textbook table tells him.

In 'melting with decomposition' the lattice melts first. The molecules, deprived of lattice support and about to decompose soon anyway, start to break up. The result is a discoloured melt, which, if allowed to cool at that point, gives a coloured solid with decomposed molecules in it. In 'decomposition with melting' the molecules decompose first. The lattice finds itself with nothing to order and falls apart, giving a deeply discoloured liquid that does not resolidify on cooling. This rich mixture melts at a much lower temperature, controlled by the 'lowered mixed-melting-point' principle. Yet textbooks confuse the two effects.

All this matters most, says Daedalus, in the industrial melting of impure mixtures, in particular in the manufacture of carbon fibres. These are made by stretching and heating a chosen pitch or polyacrylonitrile. Daedalus reckons that the ultimate performance of such fibres depends on the amount of polymeric carbon nanotube in them. Such tubes are much stiffer than steel, if not quite as strong for their weight.

If the lattice falls apart first, a useless mass of small molecules results. But if the molecules decompose first, there is a good chance that their product will be carbon nanotube, to be ordered by the surviving, stretching lattice. Polyacrylonitrile, sadly, has to eliminate ammonia to have any chance of forming carbon nanotubes; a tricky reaction. So DREADCO chemists are exploring other carbon-fibre reactions. They are heating polymers such as polyacrylamide and polyacrylic acid derivatives, hoping to find a reaction that gives more carbon nanotube and at a lower temperature. The stretching, orienting lattice could be an entirely different polymer; it might even be good old pitch. If they succeed, stronger carbon composites should soon result. This will lead to better fighter planes and fishing rods, more reliable cases and golf clubs, and stronger cars and computer casings. Even if they fail, Daedalus's chemists will still observe melting points with a clearer insight than current textbooks. David Jones