manuscript in preparation). Clearly, this is much more compatible with the kind of anisotropy needed to explain the modes. Indeed, Tromp demonstrates that it is possible to find models that provide convincing fits to both mode and travel-time data sets.

Not surprisingly, there are still some puzzles. For example, all records that show anomalous DF–BC differential times have DF waveforms that are unusually small in amplitude and unusually complicated (this might explain why they have not been noticed before). As yet there is no satisfactory explanation for this. Also, a few modes are still poorly fitted and require further study. Overall, though, the hypothesis that strong inner-core anisotropy exists near the top of the inner core now seems to be on firm ground. Perhaps the biggest remaining puzzle is its cause. A major cause of anisotropy in the Earth's mantle is thought to be alignment of anisotropic crystals by convective flow. It is extremely likely that the inner core is undergoing solid-state convection and, until recently, it was accepted that the crystal structure of iron at inner-core pressures would be anisotropic, so making this a good candidate explanation[13]. In the past year, revisions to the high-pressure phase diagram of iron have been suggested, and it is not yet clear whether inner-core material can be anisotropic. Another possibility is that anisotropic fabric has been frozen into the inner core as it solidifies from the outer core.

Strong anisotropy is just one of many unusual properties of the inner core to be explained (others include strong and possibly frequency-dependent attenuation, and an unusual Poisson ratio) and provides one more clue to the origin and evolution of this most enigmatic part of the Earth. □

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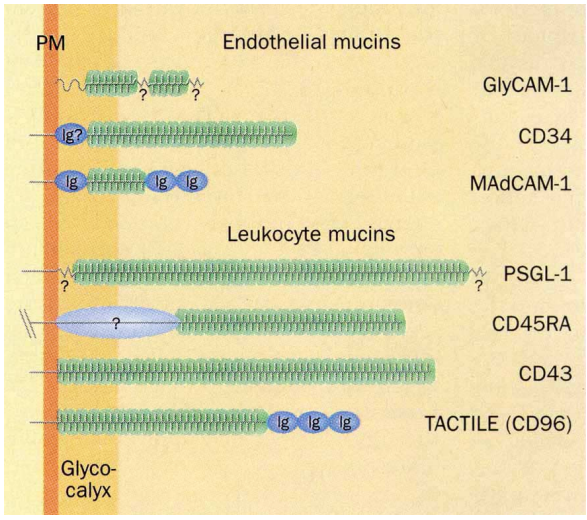
CELL ADHESION

Mucins in the mainstream

Yoji Shimizu and Stephen Shaw

THE selectin family of carbohydrate-binding proteins has a singular role in initiating the 'adhesion cascade' by which leukocytes move from the blood stream into tissue[1]. Two molecular partners for selectins have already been identified[2,3], and this week we have two more[4,5]. All are the heavily *O*-glycosylated proteins known as mucins, and mucin versatility is illustrated by Berg and colleagues on page 695 of this issue[4] — their findings suggest that a mucin domain and an integrin-binding domain, present in a single molecule called MAdCAM-1, cooperate in adhesion.



Some of the mucins present on endothelial cells and leukocytes. The immunoglobulin (Ig) domains are indicated; the potential Ig domain in CD34 is smaller than a prototypic Ig domain. A question mark indicates a region without homologies to known structures. The overall length of molecules is estimated from known properties of homologous molecules, and the surface of a typical glycocalyx is shown at 10 nm (100 Å) above the plasma membrane (PM).

The immunological incentive for studying selectins is their involvement in the movement of circulating cells such as lymphocytes and neutrophils to various places in the body[1]. For example, L-selectin helps in the migration of lymphocytes into peripheral lymph nodes and sites of chronic inflammation, as well as neutrophil influx into acute inflammatory sites. The critical interaction that allows leukocytes to leave the circulatory highway is with endothelial cells, whether they be the specialized high endothelial venules (HEV) involved in lymphocyte migration into lymphoid organs or activated vascular endothelial cells at a site of injury.

Although L-selectin was initially thought to be a homing receptor which itself could mediate a specific pattern of lymphocyte migration, it is now seen as one element in achieving specific migration. The consensus model now has it that selectins initiate weak tethering to the endothelium, which is followed by activation of strong shear-resistant adhesion mediated by integrins[6,7]. The specificity of the final process depends, combinatorially, on the specificity at each of its three steps, and therefore diversity in selectin ligands contributes in a multiplicative fashion to specificity of the entire cascade.

During the past 18 months three L-selectin ligands and one P-selectin/E-selectin ligand have been cloned, all of which are mucins. The first L-selectin ligand was GlyCAM-1, which contains two regions rich in serine/threonine that are extensively *O*-glycosylated[2]. The requirement for GlyCAM-1 sulphation for function[8], and the almost exclusive expression of GlyCAM-1 in lymph node HEV, fulfilled expectations that here was an L-selectin ligand. But L-selectin also recognizes a molecule of M_r 90K, which has been identified as the sialomucin CD34 (whose only previous claim to fame was as a useful marker for pluripotent stem cells in the bone marrow). CD34 is also expressed on endothelium but, unlike GlyCAM-1, its expression is not restricted to lymph nodes.

MAdCAM-1 was not expected to be an L-selectin ligand, because it is found primarily on endothelium in mucosal tissue and participates in specific homing of lymphocyte subsets to mucosal tissue[9]. Functional studies demonstrated that MAdCAM-1 is a ligand for the $\alpha 4\beta 7$ integrin, which had previously been implicated in lymphocyte homing to the gut[10]. Not surprisingly, cloning of the MAdCAM-1 gene revealed the presence of two amino-terminal immunoglobulin-like domains similar to domains in two other integrin counter-receptors, ICAM-1 and VCAM-1 (ref. 9). What was surprising was that MAdCAM-1 also contains a mucin-like domain.

Berg and co-workers[4] have pursued this serendipitous finding and now show that MAdCAM-1 is also a ligand for L-selectin. Like other selectin ligands, MAdCAM-1 supports the low-affinity interaction of L-selectin$^+$ $\alpha 4\beta 7^-$ cells under shear (fluid flow) that manifests itself as

'rolling' of cells along a MAdCAM-1-coated surface. So MAdCAM-1 has the structural requirements to contribute to both the rolling and strong adhesion steps of the adhesion cascade for the same cell. Although it has not been formally demonstrated, this concept has tremendous appeal because it is reminiscent of the multiple domains found in other molecules (for example the adhesive domains in extracellular matrix proteins such as fibronectin, and the SH2/SH3/kinase domains in tyrosine kinases).

Given the multiplicity of L-selectin ligands, it might seem that the protein cores of these molecules would be functionally interchangeable or degenerate. But a report of the cloning of PSGL-1, a ligand for P-selectin (and E-selectin)[5], shows that this is not the case. P-selectin-dependent binding requires expression of the PSGL-1 protein core and cannot be replaced by expression of a similar mucin core protein, CD43. So mucins are ligands not only for L-selectins but also for other selectins, and the protein core helps dictate the specificity of the interaction.

What are mucins and why are they selectin ligands? The defining characteristics of GlyCAM-1, MAdCAM-1, CD34, PSGL-1 and other mucins (see figure) is a high local density of *O*-linked sugars[11]. Prototypic mucins like CD43 (sialophorin, leukosialin) consist primarily of such regions. But in most cases mucin domains of variable sizes are interspersed with other structural motifs, giving rise to potential combinatorial effects. Notably, in three of the cases illustrated in the figure, mucin domains occur with immunoglobulin domains, meaning that the adhesive collaboration proposed for MAdCAM-1 may be a general feature of these molecules.

The dense array of *O*-linked side chains in mucins has at least two important structural implications. The first is extended structure; the average extension per amino acid is predicted to be 2.5 Å, making many mucins long enough for them to gain exposure above the glycocalyx (the glycoprotein and polysaccharide covering that surrounds cells). The second is optimal exposure and high multiplicity of the terminal sugars. These two features make mucins powerful two-edged swords: they are both anti-adhesive and pro-adhesive. By virtue of their negative charge and extended configuration, mucins act as a repulsive barrier around a cell. However, when an opposing cell has specific receptors for the mucins' sugars, adhesion supplants repulsion; such rapid interactions of lectins with mucins serve as the molecular brake which slows down leukocytes under conditions of shear[12], and initiate the first embrace between sperm and unfertilized egg[13].

Mucins play numerous tricks to increase their versatility in regulating adhesion. First, expression of the core protein is regulated, as illustrated by GlyCAM-1. Second, mucin domains are subject to alternative splicing, for example in CD45, allowing mucin function to be regulated independently of the rest of the molecule. Third, the structure of the *O*-linked side chains is regulated by cell-specific differences in glycosyltransferase expression. For instance, at some sites MAdCAM-1 fails to function as a L-selectin ligand because it is not decorated with the critical carbohydrates necessary for recognition. And fourth, there are the tricks related to anchorage to the plasma membrane: GlyCAM-1 lacks a classic transmembrane region, and its attachment to the endothelial cell surface occurs through an incompletely defined mechanism which facilitates shedding of GlyCAM-1; others undergo cleavage from their transmembrane tails.

Like most findings in cell adhesion these days, the selectin/mucin story is a glorious illustration of regulatory complexity begetting exquisite specificity. The tasks in hand are understanding fully how that specificity comes about, and defining the functions of the many other mucins. □

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PLANT EVOLUTION

Time for the angiosperms

Peter R. Crane

ANGIOSPERMS, the flowering plants, are the most diverse group of plants on the planet and in the past 25 years there has been extraordinary progress in understanding their early evolution. No single idea has been more influential in guiding research than the conventional view that angiosperms first appear in the fossil record about 130 million years ago and underwent their initial radiation through the mid- and late Cretaceous. This basic tenet of palaeobotanical research is now challenged by Bruce Cornet, who in a paper in *Modern Geology*[1] describes the discovery of putative angiosperm fossils in late Triassic rocks from eastern North America. If these specimens are angiosperms they would be more than 200 million years old.

From even the most casual overview of the plant fossil record, it is obvious that a considerable diversification of angiosperms occurred through the early and mid-Cretaceous, but for many years this interpretation was confused by records of supposed pre-Cretaceous angiosperms and the apparent diversity and modernity of Cretaceous taxa. Together, these factors fuelled speculation about a long period of 'cryptic' angiosperm evolution before their appearance in the fossil record. In 1960 an influential paper by Scott, Barghoorn and Leopold[2] questioned, and in some cases debunked, many of the pre-Cretaceous angiosperm claims. Comparison of fossil angiosperms with their supposed living relatives also called into question the assumed diversity and modernity of Cretaceous taxa[3], and with new information on fossil angiosperm pollen and leaves[4–6] made a long period of cryptic evolution seem unlikely.

This view has held sway ever since. But the possibility of a substantial pre-Cretaceous record has been raised again, from molecular-clock calculations[7,8] and also cladistic hypotheses that link angiosperms with Bennettitales (an extinct group of Triassic–Cretaceous seed plants) and Gnetales[9,10]. Because both of these potential angiosperm sister groups were present by the Triassic, the implication is that the lineage leading to angiosperms (stem angiophytes[11]) must have already diverged by at least 230 million years ago.

Enter Cornet, who in a series of papers has vigorously resurrected the possibility of the existence of pre-Cretaceous angiosperm-like plants. His evidence is dispersed fossil pollen[12], including that of the 'Crinopolles' group[13], reproductive structures attached to *Sanmiguelia*-like leaves[14] and now a dicot-like leaf and two putative angiosperm reproductive structures from the late Triassic (late Carnian[1]).

These new specimens are preserved in black lacustrine shales from the Cow Branch Formation (Newark Supergroup) of the Dan River/Danville Basin of North Carolina and Virginia. The leaf is small and clearly shows reticulate venation