SIALYL LEWIS X AND NEUTROPHIL AGGREGATION

To the Editor:

We read with great interest the report by Simon et al. about the obligatory role of \( \beta_2 \) integrin and L-selectin in neutrophil aggregation. Monoclonal antibodies against adhesion molecules (IB4-anti CD18 and DREG 200-anti L-selectin) markedly decrease aggregation. Furthermore, neutrophils from LAD I patients (CD18 deficiency) do not aggregate unless mixed with control cells, validating the role of L-selectin and \( \beta_2 \) integrin in the aggregation response. However, it remains unclear whether these adhesion molecules interact on opposing cells, or whether they are sequentially engaged in neutrophil aggregation, as in the case of adhesion to endothelial cells.

We have studied the aggregation of neutrophils in patients with the newly described adhesion molecule defect LAD II. These patients have recurrent infections and marked neutrophilia. They are deficient in Sialyl Lewis X, the ligand for selectins, and this is because of a general deficiency in fucose. Although the expression of CD18 and L-selectin in patients' cells is normal, in a static assay, the homotypic aggregation of patients' neutrophils was found to be absent (Fig 1B) compared with normal control neutrophils (Fig 1A).

Recently, it was shown that Sialyl Lewis X is essential for the adhesiveness of L-selectins. In our patients' cells both adhesion molecules, \( \beta_2 \) integrin and L-selectin are normally expressed, but still no homotypic aggregation was observed. This finding seems to indicate that Sialyl Lewis X and/or other fucosylated structures play an important role in the normal aggregation response. This observation and those reported by Simon et al. may help to clarify the role of these molecules in neutrophil aggregation. One could speculate that a sequential mechanism of recognition is indeed responsible for the aggregation response. Initially L-selectin recognition of Sialyl Lewis X (or other fucosylated counter-structures) initiates cell-to-cell binding, which is then strengthened by \( \beta_2 \) integrin in a process that is very similar to neutrophil-endothelial interaction.

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Fig 1. Homotypic aggregation of neutrophils from control (A) and LAD II (B). Note absence of aggregation and decreased flattening in LAD II.
REFERENCES


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Sialyl Lewis X and neutrophil aggregation [letter; comment]

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