Ectocytosis of intracellular antigens might be one of the pathways that triggers autoimmune disorders- A tentative hypothesis.

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Scleroderma is one of the well-studied autoimmune disorders, which involves one or more than one subpopulation(s) of anomalously activated fibroblasts. In our earlier studies, we have shown specific prevalence of antibodies to both topoisomerase I and centromeres in patients with scleroderma. We also found an increased occurrence of chromosome breakages in those patients. These data suggest that intracellular antigens might play an important role in the pathogenesis of scleroderma. The exact pathway by which the intracellular antigens get out of cells, howerver, remains to be enigmatic. Previously, we have demonstrated that ectocytosis of a specific subset of celllular proteins in the form of enriched membrane vesicles can be triggered from human skin fibroblasts cultured in a three-dimensional collagen lattice. To see if any of the intracellular antigens might be dumped out of cells by way of ectocytosis, vesicles released by scleroderma fibroblasts were isolated, resolved on SDS-PAGE and immunoblotted with sera from 80 autoimmune patients and 10 normal volunteers. Three major polypeptides with apparent molecular weight of 12-14 kDa, 32-34 kDa, and 70-80 kDa are prominent bands on both SDS-PAGE and immunoblots. Among which, the 32-34 kDa polypeptide has been further identified to be a member of the annexin protein family. While the 70-80 kDa protein has just recently been shown to be reactive to patients' antisera and rabbit polyclonal antibodies to topoisomerase I. In conclusion, we propose that ectocytosis might be one of the pathways for cells to send out intracellular antigens and subsequently causing autoimmune reactions.