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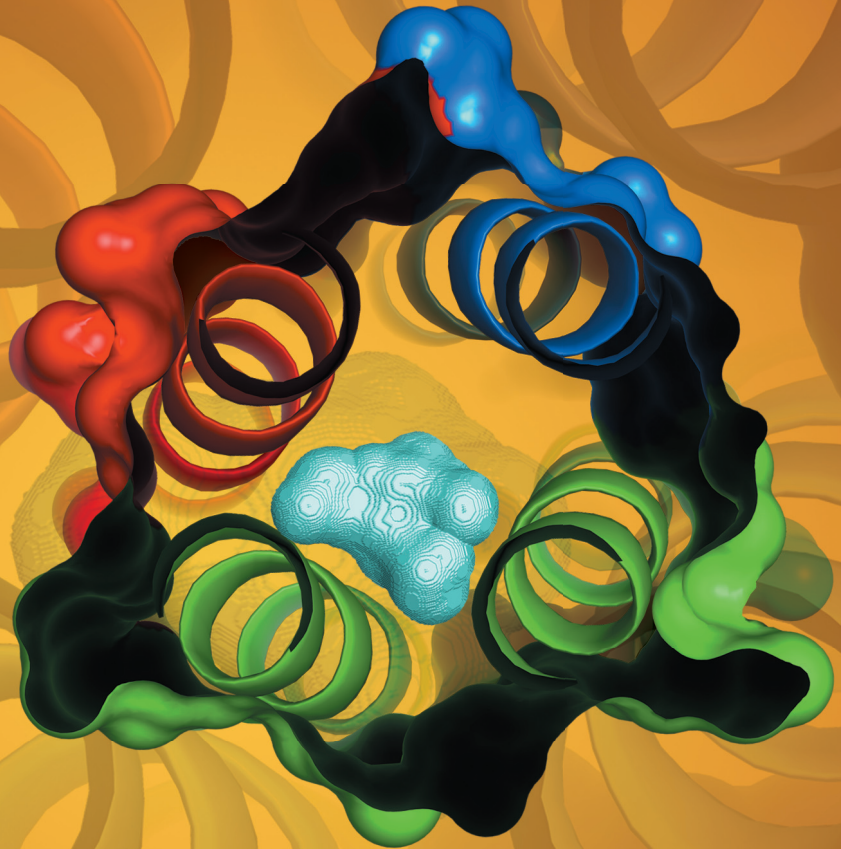
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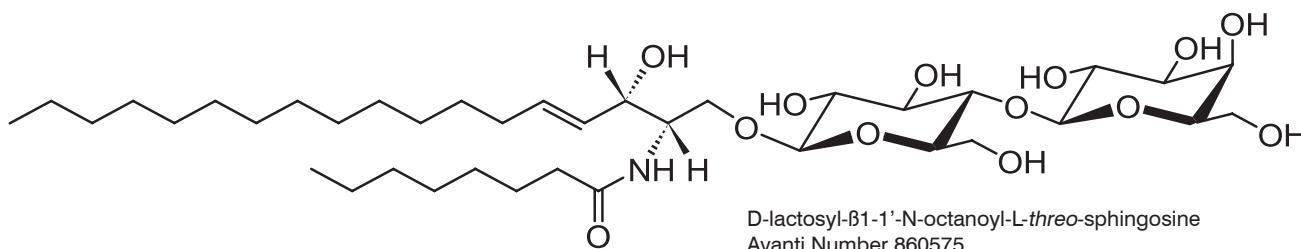
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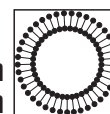
AVANTI'S NEW SYNTHETIC CAVEOLAR UPTAKE INHIBITOR



Caveolar endocytosis is an important mechanism for the uptake of certain pathogens and toxins and also plays a role in the internalization of some plasma membrane (PM) lipids and proteins. However, the regulation of caveolar endocytosis is not well understood. We previously demonstrated that caveolar endocytosis and beta1-integrin signaling are stimulated by exogenous glycosphingolipids (GSLs). In this study, we show that a synthetic GSL with nonnatural stereochemistry, beta-D-lactosyl-N-octanoyl-L-threo-sphingosine, (1) selectively inhibits caveolar endocytosis and SV40 virus infection, (2) blocks the clustering of lipids and proteins into GSLs and cholesterol-enriched microdomains (rafts) at the PM, and (3) inhibits beta1-integrin activation and downstream signaling. Finally, we show that small interfering RNA knockdown of beta1 integrin in human skin fibroblasts blocks caveolar endocytosis and the stimulation of signaling by a GSL with natural stereochemistry. These experiments identify a new compound that can interfere with biological processes by inhibiting microdomain formation and also identify beta1 integrin as a potential mediator of signaling by GSLs.

Singh, R.D., E.L. Holicky, Z.J. Cheng, S.Y. Kim, C.L. Wheatley, D.L. Marks, R. Bittman, and R.E. Pagano. (2007).

Inhibition of caveolar uptake, SV40 infection, and beta1-integrin signaling by a nonnatural glycosphingolipid stereoisomer. *J Cell Biol* 176:895-901.



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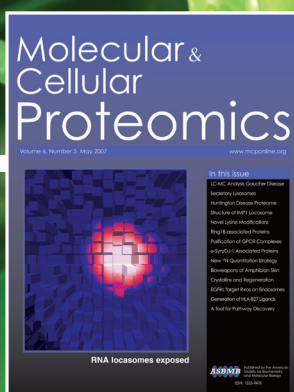
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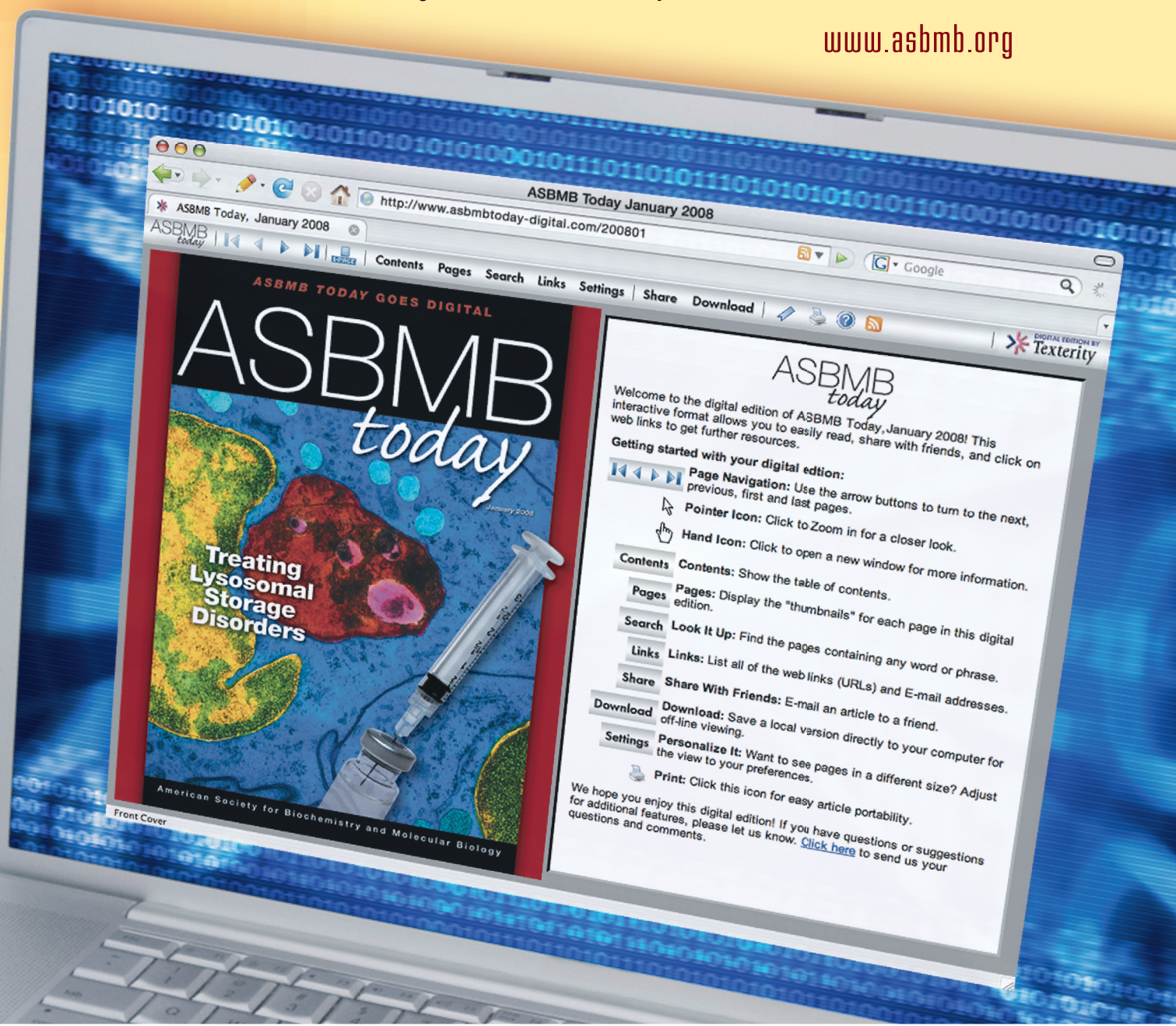
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The yeast SNARE complex shown as a surface and ribbon representation with an internal cavity. Snc1 is shown in blue, Sso1 in red, Sec9 in green, and the internal cavity in cyan. Picture was generated in Pymol. For details see the article by Strop *et al.*, pages 1113–1119.

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A photograph of two scientists in a laboratory setting. A woman on the left, wearing safety goggles and a white lab coat, is looking down at a piece of equipment. A man on the right, also wearing safety goggles and a white lab coat, is holding a round-bottom flask containing a green liquid. The background is slightly blurred, showing laboratory equipment.

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