NANO HIGHLIGHT
The Development of Vault Nano Capsules

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Scientists at the University of California, Los Angeles are using molecular engineering of a naturally occurring cellular structure called a vault to develop a flexible, targetable nano-scale capsule.

Vaults are abundant cellular particles of unknown function found in nearly all eukaryotes (cells containing a nucleus). Cryo-electron microscopy combined with single particle reconstruction has provided overall dimensions of the vault at 42 x 75 nanometers (a nanometer is a millionth of a meter). These measurements indicate that the vault is larger in mass and size than many viruses. The overall structure of the intact vault is like a hollow barrel with two protruding caps and an indented waist (Fig. 1) with a very thin shell surrounding an internal cavity large enough to encompass several hundred proteins. Thus, the vault particle is a nanocapsule with incredible potential for compound encapsulation, protection, and delivery.

Using a well-characterized insect virus into which a cloned gene can be easily inserted, it is possible to produce large quantities of a given protein in cultured insect cells. Leonard Rome and his colleagues have used this system to produce large quantities of the major vault protein (MVP). Interestingly, the protein is able to self-assemble into vault-like particles. These MVP-only vaults are somewhat irregular, often containing distorted caps. However, they have recently demonstrated that co-production of all three vault proteins (MVP, TEP1 and VPARP) in insect cells results in self-assembly of particles that appear identical to naturally occurring vaults.

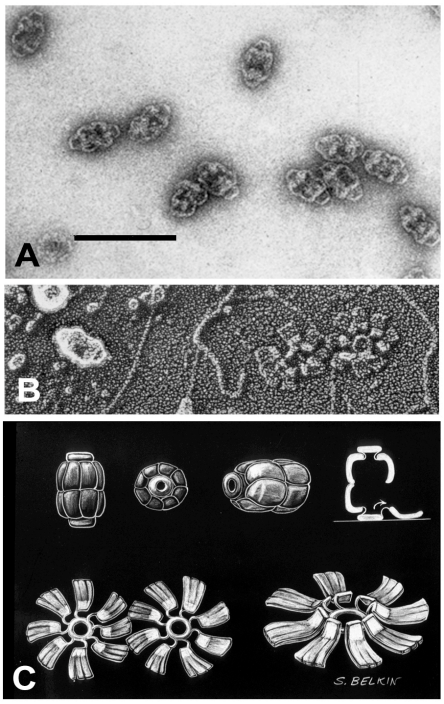

Figure 1. (A & B) Electron microscope images of vaults. Bar, 100 nM. (C) An artist's model of the vault, in both open and closed states.

By using molecular genetic techniques to modify the gene encoding the major vault protein, vault proteins have been produced with chemically active peptides attached to their sequence. These modified proteins are incorporated into the inside of the vault particle without altering its basic structure. The UCLA scientists propose to produce modified vault particles in order to test the concept that vaults can be bioengineered to allow their use in a wide variety of biological applications including drug delivery, biological sensors, enzyme delivery, controlled release, and eventually as parts for nano-electrical machines.

References:

[1] For further information about this project visit the vault website at www.vaults.arc.ucla.edu or email Leonard H. Rome at: lrome@mednet.ucla.edu

[2] Stephen, A.G., Raval-Fernandes, S., Huynh, T., Torres, M., Kickhoefer, V.A., and Rome, L.H.: Assembly of vault-like particles in insect cells expressing only the major vault protein *J. Biol. Chem.*, 2001. 276: 23217-23220.