ORGANIC SEMINAR

Professor Giovanna Ghirlanda
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Tuesday, April 13, 2010
3:30 p.m.
1315 Chemistry

Structure-based Design of Artificial Lectins

Cyanovirin-N (CV-N) is a small (11 kDa) lectin isolated from cyanobacterium *Nostoc ellipsosporum* with potent virucidal activity against human immunodeficiency virus (HIV). The antiviral activity is mediated via high affinity interactions with the high mannose oligosaccharides linked to the viral surface envelope glycoprotein gp120. This unique mode of action has spurred extensive structural and biophysical studies of the protein and its interaction with oligosaccharides.

Work in our lab has shown that multivalent interactions with oligomannosides on the surface of gp120 are necessary in mediating the antiviral activity of cyanovirin, and that such multivalency could be exploited to design improved versions of the protein. Specifically, we designed a multivalent analog of cyanovirin, NestedCVN, which contains four glycan binding sites. The protein binds gp120 ten times tighter than wt CV-N, as assessed by ELISA; antiviral tests are pending. We are currently using directed evolution to select variants of cyanovirin with tailored affinity for either oligomannose or other glycans of biological interest. Novel cyanovirin-based lectins with altered specificity will find applications as artificial antibodies for the recognition of changes in glycosylation states associated with diseases such as cancer.