Synthetic Polymer Complements and Their Applications

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A new approach has been developed to synthesize molecular complements that precisely map the size, shape, and surface characteristics of selected molecules or entities (the targets). Such synthetic polymer complements (SPCs) are unique in that they possess molecular dimensions, leading to potential utility in several significant applications. Alnis has developed SPCs for enzyme stabilization in non-aqueous and elevated-temperature environments via molecular scaffolding. Specially prepared SPCs may be used to recognize and sequester contaminants or infectious agents from complex fluids. Additionally, SPC-target conjugates also hold the promise for the delivery of therapeutic agents that are intrinsically fragile or difficult to uptake. Finally, the SPCs themselves may exhibit biological and pharmacological activities as a result of their affinity toward selected targets.

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Alnis is a start-up company developing advanced bio-entities based on target-directed synthesis. The technical foundation of Alnis is its novel approach of target-mediated direct synthesis of nano-structures and macromolecular networks, whose three dimensional topography (surface contours and energetics of localized points of interaction distributed on such surfaces) forms precise complements of selected targets. Example "targets" include small stereo-specific drug molecules, peptides, cytokines, cell receptors, viruses, bacteria, cancer cells and other biologically and pharmacologically active nano-structures and assemblies.

Target-directed synthesis is enabled by the creation of specialized building block molecules. These molecules possess heads (where affinity interactions reside with selected sites on the target), tails (which may be long or short, linear or branched, depending on packing requirement, hydrophilic or hydrophobic, depending on the environment in which the finished material will serve), and crosslinkable functional groups. When introduced into a properly prepared medium containing the target, the heads of the building blocks congregate around complementary sites on the surface of the target, while the tails cause “self assembly”, forming a monolayer on the target. Crosslinking of the functional groups then produces a precise macromolecular complement of the target surface. The resulting entity, termed Synthetic Polymer Complements (SPCs), have dimensions comparable to that of the target. Hence, the

uniquely engineered SPCs are essentially “molecular molds” of the chosen targets from which they are synthesized.

After formation and separation from the template structure, SPCs may be used in a multitude of applications. Current research funded through DARPA focuses on the use of SPCs to incapacitate pathogens that may be used in biological warfare. Also, an NCI-funded program focuses on cancer diagnosis and therapy. Additional diagnostic and therapeutic applications are a direct extension of the above projects. Other applications enabled by the SPC technology include small molecule (such as chiral drug) separation and purification.

As discussed above, the template used for SPC formation is removed prior to use. Alternatively, an SPC-target conjugate may be the desired product. When the targets are enzymes, the SPC "cage" serves to protect the enzyme against thermally triggered and media induced denaturation. Hence, these naturally occurring catalysts can find a host of applications in high temperature and non-aqueous environments. Early laboratory results indicate the promise of this molecular scaffolding approach. Alnis will next exploit the benefits of SPC-target conjugation for protected drug delivery, such as fragile therapeutic peptides and difficult-to-uptake drug candidates. In addition to protected drug delivery, the SPCs themselves may exhibit diagnostic and/or therapeutic activities as mentioned above. Hence, the work at Alnis has potential impact on a number of areas of the pharmaceutical industry.