Next Generation Therapeutics, Antibiotics and Antivirals

Leader: Dr. Chris Diehnelt

Team: Chris Diehnelt, Craig Crews (Yale)(tentative), Stephen Albert Johnston, Neal Woodbury

Summary: CIM scientists are committed to developing new ways to detect disease early. But this effort must be accompanied by one to develop the treatments for the disease. Synbodies were invented to meet this challenge.

Synbody Therapeutics: The drug industry has largely relied on small molecules, natural or synthetic, as its source for treatments. Though relatively cheap to produce once identified and easy to administer, small molecules are inherently non-specific in binding leading to side-effects and/or loss of efficacy. For these reasons this historical phase of the pharmaceutical effort is coming to an end. It is being replaced by targeted therapeutics. Most of these are antibodies, now 70% of the new drug pipeline. However, antibodies are large (do not go into cells), expensive and unstable. A single course of Herceptin treatment can cost $80,000. Because of these liabilities antibodies will not be the source of drugs for the developing world. What are needed are drugs that are highly specific, versatile in design, inexpensive and can enter cells. Synbodies were invented to meet these requirments.

CIM scientist have developed a process over the last few years where the production of synbodies to any target can be standardized. The target is applied to the peptide arrays we developed, under any condition desired. Several peptides that bind the target are chosen and then combined in various combinations to find the optimal pair. These synbodies can be simply modified to meet any specification required. The result is a small molecule with the specificity of antibodies that is cheap to produce. We have shown that some, at least, of the synbodies enter cells to bind their target. Synbodies are probably the best new approach to therapeutics

We are also facing a crisis in antibiotics. Antibiotics are losing effectiveness far faster than we are developing new ones. In addition we have no effective anti-virals for acute infection. We have demonstrated that synbodies could also be key to solving these problems.

Synbody Antibiotics: It is widely recognized that there is a crisis in producing effective antibiotics. Broad spectrum antibiotics have had a huge positive impact on human well-being but have fostered wide spread bacterial resistance. With a crisis looming in this regard there is little hope that current approaches can produce 20 new antibiotics by 2020 as called for by the Infectious Disease Society of America. Compounding the problem, there is increasing evidence that the endogenous gut bacteria that are also killed by current antibiotics do significant good for our health. Not to mention that we also have a dearth of antiviral, antifungal and antiparasitic drugs. We have evidence that the synbody system could solve this problem.

We have shown that bacteria, viruses and cells can be applied to the peptide arrays we developed and peptides chosen that bind to them. For bacteria we have shown that killing peptides can also be selected. The targeting and lytic peptides can be combined to form an antibiotic. In addition, features

can easily be added to the synbody to recruit natural killing functions. The ability to target specific bacteria opens a whole new frontier of targeted antibiotics that would relieve both the problems of antibiotic resistance and killing helpful bacteria. The same protocol can be applied to viruses and even mammalian cells.

Value proposition:

CIM scientists have demonstrated the potential value the synbody platform for both therapeutics and anti-infectives. The arrays that are key to the platform have been developed and are in production.

Collaboration objectives:

Key collaborators will be with expertise in animal models for therapeutics and anti-infectives. Collaborators with interest and expertise in pharmacology will be essential. Clinical researchers with background in clinical trials will be required.

Contact: Chris Diehnelt Stephen Albert Johnston

Chris.diehnelt@asu.edu Stephen.johnston@asu.edu