NIH expands recombinant DNA guidelines to include synthetic nucleic acid molecules
By Ryan P. Schlimgen

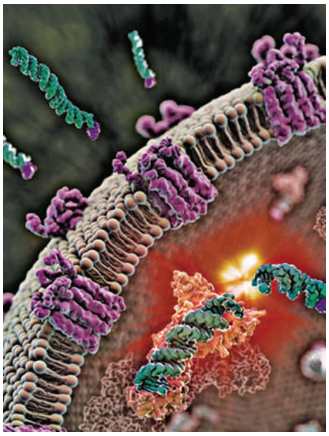
In 1974 Paul Berg performed the first experiments cleaving and ligating viral DNA; demonstrating the awesome power of genetic manipulation while raising serious safety concerns and necessitating national regulations and safety standards. A year later at the Asilomar State Beach in California a group of leading biologists, lawyers, and physicians met and set the ground work for regulations and safety standards for recombinant DNA. The core principles of the conference, which include containment as an essential consideration in experimental design and matching safety practices to the inherent risk of procedures, were then adopted in 1976 by the NIH Office of Biotechnology Activities (OBA) in the *NIH Guidelines for Research Involving Recombinant DNA Molecules.* These *NIH Guidelines* set out the responsibilities of the Principal Investigator (PI), established the Institutional Biosafety Committee (IBC), and principal of expert review of all recombinant DNA work at an Institution.

In the intervening 37 years all research involving recombinant DNA in academic and commercial institutions that receives grants and funds from the NIH has been reviewed by an IBC. However, in those same 37 years the understanding and the science of nucleic acids has outpaced the regulations. It is now possible to synthetically create and manipulate nucleic acids sequences in ways only possible in the past through recombinant technologies. With this advanced understanding of recombinant technologies and to manage the changes in the science, on March 5, 2013 the NIH has expanded NIH Guidelines to include synthetic nucleic acid molecules. This regulatory expansion was driven by recommendations from the National Science Advisory Board for Biosecurity (NSABB) and recognition that containment of recombinant nucleic acid molecules is critical regardless of the technology used to generate the nucleic acid molecules.

As a result of these changes the *NIH Guidelines* define recombinant and synthetic nucleic acid molecules as molecules that are constructed by joining nucleic acid molecules and can replicate in a living cell. In addition, they include nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules. And finally, the *NIH Guidelines* also cover the molecules that result from the replication of recombinant and synthetic nucleic acid molecules. Therefore all experiments using synthetic nucleic acid molecules will be covered by the NIH Guidelines and require IBC review of the research project.

As expansive as these new definitions are, there are some exemptions to research involving synthetic nucleic acid molecules from OBA and the IBC regulation. First, a growing area of research uses short synthetic nucleic acid sequences to transiently reduce or suppress the expression of target genes called RNA interference; these experiments will not be regulated. Second, synthetic nucleic acid sequences that will not integrate into the DNA of the host organism will not be regulated. Third, synthetic nucleic acids sequences of single nonchromosomal or viral DNA source that exists in nature will not be regulated. Finally, the chemical synthesis of nucleic acids that is not placed into an organism will not be regulated. However, the existing requirements to review recombinant DNA research that were previously covered under the NIH Guidelines have not changed.

Despite the changes to the regulation of recombinant and synthetic nucleic acid molecules, the process of IBC review of research projects has not changed. The IBC continues to follow the core principles of the first Asilomar Conference ensuring that the laboratory design, containment procedures, and safety practices are suitable to the inherent risk of research being performed. The PIs continue to supervise laboratory staff to ensure that the required safety practices and techniques are employed. Together they ensure the cutting edge scientific research here at Tufts is performed safely and in compliance with federal regulation.



synthetic DNA entering a nucleus

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DNA synthesizer