Development of a Novel Solid Support Linker for Oligonucleotide Synthesis.

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The breakthrough in oligonucleotide synthesis has been the development of the phosphite triester by Letsinger and co-workers and the development of phosphoramidite chemistry by Beaucage and Caruthers. This together with the automated synthesis on “Gene Machines” have made it possible to routinely produce oligonucleotides in large quantities in a short period of time. However, the drawback in today’s oligonucleotide synthesis is the lengthy deprotection time. After the oligonucleotide is synthesized it is cleaved from the solid support and deprotected in solution, a process that can take days, particularly in RNA synthesis.

In our lab we have developed a novel photolabile linker for the solid-phase synthesis of oligonucleotides that allows one to keep the oligomer on the solid support throughout the whole synthesis, including all the deprotection steps. With this novel linker, the time needed for the post synthetic steps is greatly reduced and the deprotection is easier to perform. When the oligonucleotide is finally released (hv), the purity is higher and the subsequent purification is easier than when using current methods. With our new linker the synthesis and deprotection of RNA and DNA oligonucleotides can be completely automated, making High Throughput Screening and similar applications possible.