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A Rational Methodology for Rapid Chemical And Enzymic Synthesis of Long Double Stranded DNA: A Human β -Interferon Gene

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A RATIONAL METHODOLOGY FOR RAPID CHEMICAL AND ENZYMIC SYNTHESIS OF LONG DOUBLE STRANDED DNA: A HUMAN β -INTERFERON GENE

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With now well established procedures for rapid chemical synthesis of oligodeoxyribonucleotides, these compounds have found widespread application in molecular biology research. In particular, the total synthesis of genes has become an attractive basis for the molecular design of proteins. Since synthetic genes have the advantage of being constructed from a set of short oligonucleotides (fragments), new gene variants can be generated conveniently by replacing some of the fragments.

We here describe a rational combination of techniques that allows the rapid synthesis of long double stranded DNA. This includes

- computer programmes for the design of those gene fragments that are best suited for straight-forward ligations, as well as for providing helpful protocols to coordinate simultaneous syntheses of oligonucleotides.
- synthesis of oligodeoxyribonucleotides following the principle of segmented solid supports.
- time saving purification procedure using disposable prepacked cartridges.
- rapid characterization of oligonucleotides by base composition dependent accurate sizing on polyacrylamide-gels with the help of homo-oligonucleotide chain length standards.

The methodology is exemplified by the synthesis of a 517 bp long DNA coding for human β -interferon.