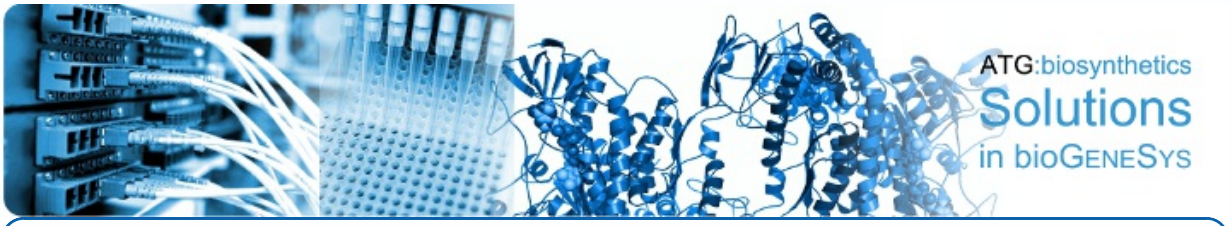

CODONEWS Issue69

Bioinformatics for Semi-Predictive Functional *in silico* designs of Synthetic Genes and Clusters become more and more reality.

Dear Customers,

You for sure know that the difference between high yield of protein expressed and the yield of small molecules are just two sides of the same coin. The specific activity of the protein is mainly dependent on the autonomous re-folding power intrinsically encoded in the amino acid sequence of a protein, the supporting activity of helper proteins like the professional Chaperons are needed. Those proteins like many membrane proteins which do not have a strong tendency for autonomous re-folding are heavily dependent on the co-translational folding properties directed by the ribosomal kinetics along the messenger RNA. There is an increasing knowledge documented in various recent publications about approaching a rational and at least semi-predictive way to handle big and complex sequences in this respect.

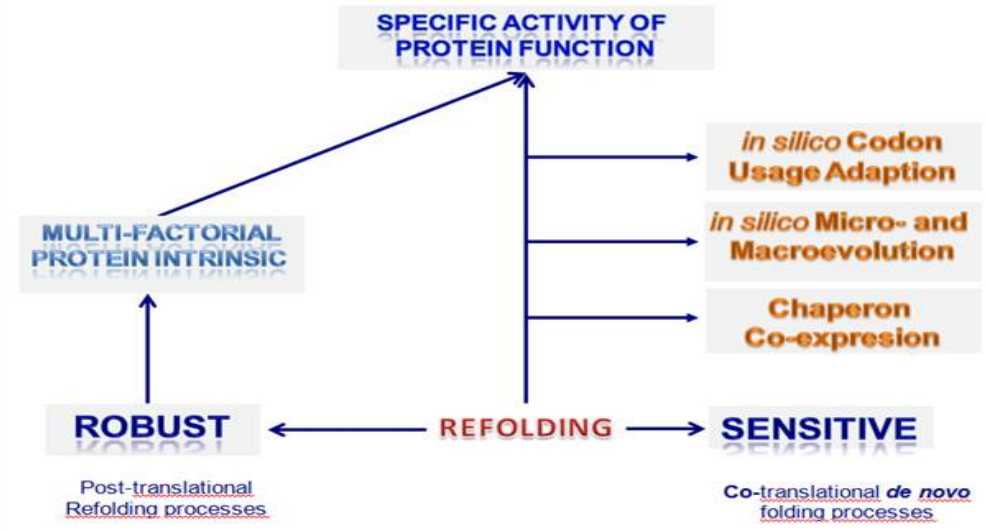

Figure-1. The proper function of proteins like enzymes is determined by its general folding properties. Correct folding into a functional protein structure can be **(1)** autonomously, supported by **(2)** Chaperones or **(3)** highly dependent from the ribosomal co-translational speed or both. Robust refolding enzymes like **RNase** (Anfinsen) have the ability for correct folding information intrinsically encoded. Therefore these are autonomously refolding into its functional structure. In contrast are the folding sensitive proteins. These fall in two classes. For the one type co-expression of chaperones which are supportive for the folding process are binding to proteins in statu nascendi for the stabilization of meta-structures which are favourable to finally promote functional folding. In parallel to protein neo-genese, co-translational folding processes can be highly dependent from the correct fine tuning of the ribosomal kinetics along the RNA message and in addition associated with chaperones. For the heterologous expression of enzymes and other proteins the adaptation of the codon usage as well as the micro and macro evolution for the creation of biodiversity and in addition the chaperon co-expression are versatile approaches for achieving a high specificactivity of the protein function like catalysts

ATG:biosynthetics is specialist in bio-synthetics pathway systems on **Pro-** as well as in **Eukaryotes**. Continuously we are developing and providing the **up-to-date** knowledge in the field mirrored in our development of algorithms.

We are offering services like :

- Detailed bioinformatics description of natural pathways by annotating structures, regulatory elements and genes.

- Biodiversity analyses for the identification of alternative genes for equal functions.
- Comparative genome analyses **for information gained from** orthologs, paralogs, genome structure
    - identification of high expression group genes
    - identification and delineation of specific sub-tables
    - balanced codon use and codon sampling
    - tRNA - adaption index calculations
    - Aminoacyl-tRNA supply and codon use demand models
- Functional genomic analyses for RNAseq, MS
- **GeneCheck** service for finding optimal gene improvement strategies
- Single and multi-gene sequence target parameter *in silico* optimizations for
    - transcriptional initiation
    - translational initiation, elongation and termination
- Various different multi-gene constructional design concepts for the exchange of genes
- Design of Experiment **(DoE)** for designing but in addition minimizing iterative improvement cycles
- Gene syntheses **with acceptable prices**
- **FlexTEC** - expression systems for generating multi-gene constructs and specific deassembly options
- **for your individual needs and requirements please inquire here**

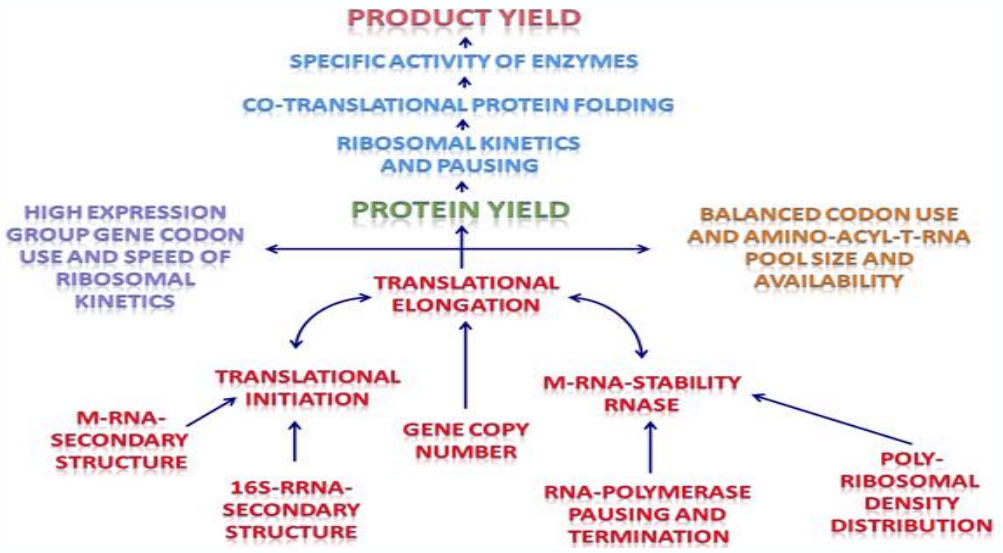

Figure-2. Different composite DNA/RNA sequence features are determining the functional gene products and the yield of small molecules . The specific activity of an enzyme is the key driver of the product yield and not the general protein yield achieved. The production yield of small molecule compounds is predominantly dependent from the balanced activity of all the biosynthetic cascade enzymes involved. So the iterative improvement of the specific activity of enzymes is the key for the proper and functional folding of the enzymes involved. It is the direct function of success for production processes to evolve it towards the aim to guarantee the highest yield of proper functional working enzymes possible.

Sincerest regards,

Dr. Hubert S. Bernauer
ATG:biosynthetics GmbH
++49-761-13776959
http://www.atg-biosynthetics.com

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