



## INNOVATION WORKS™

Technology from the European Molecular Biology Laboratory

# ESPRIT – Systematic approach for generating soluble protein variants

EMBLEM Ref. 247

### Challenge

- proteins often express insolubly which limits their ability to be structurally analysed by crystallography and NMR
- current methods use huge tags as “solubility reporters” leading to a high number of false positive results in a screen

### Commercial Opportunity

- technology transfer of the platform on a license basis
- screening services

### Technology

- allows all possible truncations of a target protein to be synthesized and screened in a single experiment
- the approach uses a small and inert peptide as solubility tag
- underlying principle is that only soluble molecules are substrates for enzymes, therefore the tag can only be enzymatically modified when fused to a soluble protein
- the method allows high-throughput analysis of an expression library of variants of individual proteins used in combination with a mutation or truncation procedure strategy

### Contact

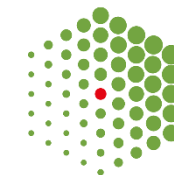
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### Intellectual Property

UK0419628.3



**EMBLEM**  
TECHNOLOGY TRANSFER

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Protein insolubility is a wide spread problem and methods for generation and screening of soluble variants address a common need. Systems have been described that aim to identify soluble protein variants by random mutagenesis or truncation. These methods usually involve fusion of a C-terminal “solubility reporter” (e.g. GFP, CAT or beta galactosidase). The tag used in the methods described above are large and thus enhance the solubility profile of the fusion product. The solubility profile of the fusion product is highly dependent on the solubility phenotype of the tag used. By using a smaller tag the solubility influence of the tag is reduced leading to a reduction of false positives.

The approach described herein allows for high-throughput analysis of an expression library of variants of individual proteins used in

combination with a mutation or truncation procedure strategy. Our approach uses a small and inert peptide as solubility tag. The underlying principle behind the use of this peptide as a solubility reporter is that only soluble molecules are substrates for enzyme. Therefore, if the peptide is fused to a soluble protein (encoded by gene x), the protein is enzymatically modified via the tag. If it is fused to an insoluble protein, no enzymatic modification occurs. As a result this method allows clones to be screened for solubility with a lower number of false positives in comparison to known methods.

## Reference

Yumerefendi et al. 2010, J Struct Biol  
doi: 10.1016/j.jsb.2010.02.021

