Complete in vivo Protein Lipidation through Dynamic Metabolic Control of Acyl-CoA Biosynthesis

Unmet Need
Protein therapeutics and biologics are becoming more common in healthcare. However, these molecules often struggle to cross epithelial barriers or cause immune reactions, necessitating either injection or direct site administration to be effective. These obstacles to treatment can be mitigated by myristoylation, by which acyl groups are attached to a protein to help it bind albumin, which facilitates its transport through epithelial barriers and the bloodstream. However, myristoylation is either conducted chemically following protein synthesis or else requires rich, detergent-heavy media. Despite being a cost and resource-expensive process, these methods are also low yield. There is a need for a more modular and high-throughput method of protein myristoylation.

Technology
Duke inventors have developed an in vivo bacterial gene expression system for high-yield protein acylation. This is to be used in generation of protein and peptide therapeutics that can more easily move throughout the body. Specifically, this technology takes advantage of two genes found in *E. coli* and repurposes them to acylate synthesized proteins. This can be used on any protein with an exposed N terminus across a variety of expression vectors. This has been demonstrated in induction and subsequent myristoylation of protein from plasmids pNAP-1 and pCDF-hNMT-1 by genetically modified *E. coli* grown without the use of specialized chemical reagents or growth media. This is currently patented and is the next step in harnessing the therapeutic potential of biologics.

Advantages
- High protein yield compared to chemical myristoylation approaches
- Does not require use of expensive rich media, detergents
- Ideal for industrial biomanufacturing use

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Meet the Inventors
Lynch, Michael
Menacho Melgar, Romel

Contact For More Info
Rasor, Robin
(919) 681-6412
robin.rasor@duke.edu

Department
Biomedical Engineering (BME)

Publication(s)

External Link(s)
- A review of lipidation in the development of advanced protein and peptide therapeutics (Journal of Controlled Release, 2019)