NASA's Astropharmacy for Biomanufacturing of Peptide and Protein Pharmaceuticals in Space and in Other Austere Environments

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The *Astropharmacy,* under development at NASA Ames Research Center, is a compact, portable technology for small-scale manufacturing of biopharmaceuticals (peptide and protein drugs). This technology is designed for rapid, on-demand drug production in austere environments. The Astropharmacy is a solution to the problem of short shelf-life for peptide/protein pharmaceuticals that NASA faces for extended duration missions to deep space, such as to the Moon and Mars. The technology uses *Bacillus subtilis,* engineered to incorporate the genetic information needed to produce the desired peptide/protein drug. *B. subtilis* is an attractive chassis organism for NASA applications because it can be sent into space in a dormant state—as a spore—making it highly resistant to heat, desiccation and radiation. When a drug is needed, *B. subtilis* spores engineered for the desired drug can be reactivated by the addition of culture medium and grown rapidly, producing a first dose in 24 hours or less. The Astropharmacy system relies on novel microfluidic technology to support the reactivation and growth of *B. subtilis* and includes provisions for novel drug purification methods based on the use affinity tags which allow for highly selective capture of the manufactured drug. An alternative embodiment of the Astropharmacy uses cell-free peptide/protein synthesis technology, which relies on cell extracts to provide all the necessary machinery to produce the desired peptide or protein drug, without the need for an intact microbe or other chassis organism. At present, the use of both *B. subtilis* as a chassis organism and the use of cell-free systems for peptide/protein drug synthesis does not allow for post-translational modification, although methods for carrying out these modifications may be available in the near future. In many instances, however, the lack of post-translational modification capability is not problematic. Many peptide and protein drugs produced in microbial systems (*E. coli,* commonly) have been shown to have adequate biological activity even in the absence of post-translational modification. Pharmaceuticals of interest to NASA, such as *Granulocyte Colony Stimulating Factor, Granulocyte-macrophage Colony Stimulating*

Factor and *Teriparatide,* are currently being explored for production by the Astropharmacy, with many additional peptide/protein drugs in the pipeline.