We are developing a novel, autonomous bioreactor that can provide for the growth and maintenance in microgravity of 3-D organotypic epithelial-stromal cultures that require an air-liquid interface. These complex 3-D tissue models accurately represent the morphological features, differentiation markers, and growth characteristics observed in normal human epithelial tissues, including the skin, esophagus, lung, breast, pancreas, and colon. However, because of their precise and complex culture requirements, including that of an air-liquid interface, these 3-D models have yet to be utilized for life sciences research aboard the International Space Station. The development of a bioreactor for these cultures will provide the capability to perform biological research on the ISS using these realistic, tissue-like human epithelial-stromal cell models and will contribute significantly to advances in fundamental space biology research on questions regarding microgravity effects on normal tissue development, aging, cancer, and other disease processes. It will also allow for the study of how combined stressors, such as microgravity with radiation and nutritional deficiencies, affect multiple biological processes and will provide a platform for conducting countermeasure investigations on the ISS without the use of animal models. The technology will be autonomous and consist of a cell culture chamber that provides for air-liquid, liquid-liquid, and liquid-air exchanges within the chambers while maintaining the growth and development of the biological samples. The bioreactor will support multiple tissue types and its modular design will provide for incorporation of add-on capabilities such as microfluidics drug delivery, media sampling, and in situ biomarker analysis. Preliminary flight testing of the hardware will be conducted on a parabolic platform through NASA’s Flight Opportunities Program.