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Antibody engineering—a valuable asset in preventing closed environment epidemics

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Abstract

Investigations of Mir, Space Shuttle, Skylab and Apollo missions report extensive colonisation of the spacecraft by bacteria and fungi, which can lead to degradative effects on spacecraft equipment and devastating effects on space-grown crops. More than 80% of terrestrial greenhouse epidemics are due to the fungal genera *Phytophthora*, *Pythium* and *Fusarium*, which have been found in life support system test-beds. The advent of recombinant antibody technologies, including ribosome display and phage display, has made it possible to develop antibodies against virtually any toxin or organism and allows for maturation of antibodies by in vitro molecular evolution. These antibodies may play an important role in an integrated pest management regime for life support systems. Efficacy of existing fungal countermeasures could be increased by chemical linkage to antibodies, which target the site of action of the biocide or trap the pathogen in a biofilter. Novel recombinant antibody–biocide fusions can be expressed in situ by plants or symbiotic microbes to create direct disease resistance.

1. Introduction

Plants will play an integral role in future bioregenerative life support systems (BLSS), for oxygen production and concomitant CO_2 removal, for waste and water recycling and for food production [1–3]. Due to limited launch mass and ease of handling, the plant systems will likely be hydroponic rather than soil-based cultures. Hydroponic test-beds have been shown to be infected with various bacteria [4,5] and with various fungi including *Fusarium* and *Pythium* [4,6,7]. During the last 30 years, both the Russian and US space programmes have shown spacecraft to be contaminated with a wide range of bacteria, fungi, oomycetes and actinomycetes [8,9].

Present attempts at controlling microorganisms in hydroponics vary in method and effectiveness. In general, hydroponic nutrient solutions are disposed of and the nutrient delivery system sanitized by chemical means before fresh nutrient solution is added. However, environmental laws are becoming stricter on nutrient leaching and researchers are focusing on recirculating nutrient delivery systems. Recirculating systems are the only option for extraterrestrial use, due to the inhibitory cost of resupply.

Antibodies are routinely used for disease detection in the form of immunoassays. The advent of hybridoma technology and recombinant DNA

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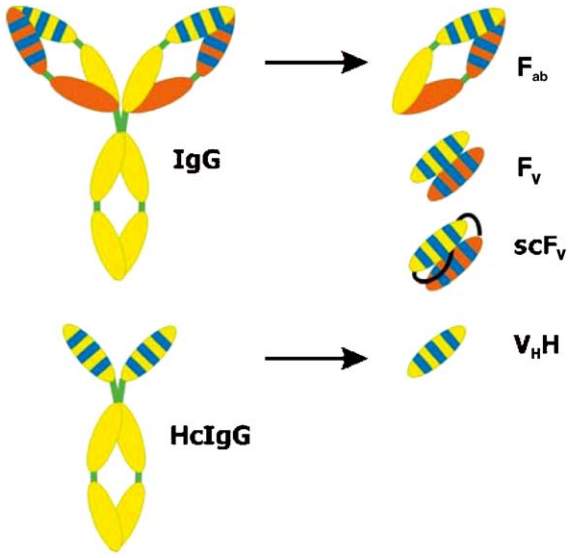

Fig. 1. Immunoglobulin G (IgG) antibody and fragments thereof. Heavy chains are light yellow, whereas light chains are dark orange. Striped domains represent the variable domains containing complement determining regions (CDRs) in blue. HcIgG refers to the heavy chain version of IgG present up to 50% of total IgG in camelids. The antigen binding fragment (F_{ab}) is a large and stable fragment, whereas the variable fragment (F_V) is an unstable association of the two original variable domains. The single chain variable fragment (scF_V) is recombinantly expressed with a linker to make it a small and stable antibody fragment. The variable heavy domain of the camelid HclgGs, called a V_HH, is stable and the smallest of all antigen binding fragments.

technology has enabled large-scale production of antibodies in vitro and thus boosted the share of antibody-based assays in the diagnostics industry to 30%, representing a US$ 3B industry [10]. It is now also possible to develop antibodies and antibody fragments (Fig. 1) for use in high throughput diagnostics, enhanced imaging techniques, cancer therapy, pollution monitoring and plant protection.

Here, we describe how antibodies are engineered for the purposes of direct maintenance of pathogen-free closed environment systems. Because of the brevity of this paper, it focuses on the contamination by, and prevention of, fungi and especially *Pythiaceous* oomycetes, which, although recently re-classified to their own kingdom [11,12], will be referred to as fungi in this paper. The antibody technology described here can equally well be applied to other microorganisms as well as inorganic toxins.

2. Contamination of spacecraft

During its 15-year operation, the Mir space station was reported to be contaminated with 25 different genera of fungi and yeasts [13]. At least 10 of these genera contain species, which are plant pathogens (Table 1) [14]. The American Skylab missions, as well as the Apollo 14 and 15 missions, were reported to be contaminated with *Aspergillus*, *Penicillium* and *Cladosporium* spp. amongst others, including for example *Aspergillus flavus* [15], which infects peanut, and *Cladosporium cladosporioides* [16] which infects corn and wheat. Schuerger [9] presents a good overview of microbial contamination of advanced life support systems (ALSS).

Contamination of ALSS testing facilities by *Pythium* and *Fusarium* species and associated diseases of plant growth systems therein have been reported [6,7,17].

The higher microbial contamination in hydroponic vs. field crops is due to how the nutrients reach the crop. A recirculating solution allows pathogens more time to grow and spread. But the most critical difference lies in the fact that hydroponic nutrient solutions contain highly soluble ions [18], which are more readily available to pathogens than complex

Table 1
Plant pathogenic genera recovered from Mir and their potential agricultural hosts [14,13]

Genus	Potential hosts
Acremonium	Sorghum
Alternaria	Peanut, sweet potato, wheat, lettuce, soybean, tomatto, beet
Aspergillus	Peanut, wheat, sorghum
Botrytis	Peanut, sweet potato, lettuce, tomato, beet
Cladosporium	Wheat
Fusarium	Peanut, sweet potato, soybean, tomato, beet, sorghum
Mucor	Sweet potato
Penicillium	Sweet potato, wheat, beet, sorghum
Sporobolomyces	Wheat
Stemphylium	Peanut, soybean, tomato, beet