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An Animal Model for Biofilm Formation by Pseudomonas aeruginosa

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Cystic fibrosis (CF) is one of the most common inheritable genetic disorders. It is caused by a mutation in the Cystic Fibrosis Conductance Regulator (CFTR), and is characterised by multiple symptoms like increased levels of extremely viscous mucus in the lung. Lungs of CF patients are usually colonised by a wide spectrum of pathogens, but the main microorganism that causes disease is *Pseudomonas aeruginosa*. By forming biofilms in CF lungs, *P. aeruginosa* protects itself against attacks from the immune system as well as against antibiotic treatment. Understanding of biofilm formation by such bacteria is a prerequisite for the development of an effective therapy for CF patients. Therefore, the establishment of an appropriate animal model would represent a great advance for research on this subject since a model is still lacking so far. Present animal experiments for chronic *P. aeruginosa* are inappropriate due to the fast elimination of the bacteria and the absence of biofilm formation.

We use a novel model system by infecting mice that bear a solid tumour intravenously or intratrachealy with *P. aeruginosa*. In these tumour tissues they are protected from the immune system and should be able to persist for an extended period of time. Indeed, the bacteria accumulated in the solid tumour and also formed biofilms, which was dependent on functional quorum sensing system. Different bacterial strains were investigated including mutant strains, which all were able to colonize the tumours. However, mutants that are not able to grow under hypoxic conditions only colonized tumour rims while wild type could reside in the tumour center. This situation to a large degree resembles the situation that the bacteria encounter in the lung of CF patients. Therefore our model system will offer the possibility to study the process of biofilm formation by *P. aeruginosa* and allows to test advanced treatment.

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