检测超可变性假单胞菌在囊性纤维化患者中的检测

从南方巴西患者

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研究的主要目的是确立超可变性（HPM）P. aeruginosa从囊性纤维化患者痰中在巴西北部CF人群中出现的频率。比较非超可变性（NHPM）和超可变性菌株在PFGE和抗生素敏感性方面。

PCR检测了 carbapenemases 在 carbapenem resistant 菌株中的存在。

这可能是一个有趣的研究所要新信息，关于在巴西CF患者（131例）中超过528例P. aeruginosa菌株的频率。这在基本层面上是宝贵的数据，使我们有可能比较P. aeruginosa菌株从不同的地理位置，以获得对超可变性P. aeruginosa在慢性感染中作用的见解。

主要强制性修订

1. 超可变性菌株的鉴定

我不确定为什么由筛选方法（根据文献7中列出的三种抗生素的抑制区中耐药菌株）获得的HPM频率（135菌株）与实际的Rifampicin突变频率（9菌株）有如此大的差异。这需要解释。应该包括PAOmutS突变的阳性对照。最近在拉丁美洲的另一项研究中已经发表了这两者之间的高相关性（Feliziani et al., PloSone, 2010, vol.5, issue 9）。

我建议提供数据关于在参考文献中列出的抑制区中的菌株数（文献7）和在135菌株中的实际突变频率。

2. 遗传表型的超可变性
Both mutS and mutL have been shown to be important for the HPM phenotype in CF P. aeruginosa isolates from various geographical regions, so sequence of mutL is also relevant for HPM with frequency of Rifampicin mutations 20 times higher than PAO1. As all the mutS mutations found in the Brazilian isolates lead to amino acid substitutions, complementation with a wild-type mutS or analysis of the sequence variability of the paired NHPM should be provided in order to show that these amino acid changes lead to a non-functional protein.

There are several publications on the type of mutations encountered in mutS in HPM P. aeruginosa from other CF centers and a comparison with their sequence variability would be interesting to be included in the discussions.

Minor essential revision

1. Analysis of longitudinal samples from the seven patients harboring the 9 HPM isolates showed that the HPM was not a stable finding and the HPM isolates had also different PFGE patterns compared to NHPM. It has been published a longitudinal study on isolates covering long period of chronic colonization (more than 25 years) and the HPM phenotype did not influenced the PFGE pattern (Ciofu et al., Microbiology, 2010, 156, 1108-1119). This suggests that the Brazilian CF patients are either in the early phases of the chronic infection as it has been shown that different clones are present in the lung until one dominant clone is established (Jelsbak et al., Infect Immun. 2007) or that the chronic PA infection in Brazilian CF patients is not monoclonal as published by other CF centers. This should be discussed in the paper.

2. The authors suggest that the low percentage of HPM found in the study is similar to what it has been reported during early colonization (this reference is missing in the text). Is it any evidence that the majority of the 131 CF patients are in the early phase of colonization?

In order to draw any conclusions on these results, a minimum of clinical information about the CF patient population is also necessary (at least % children vs. % adults).

Discretionary revisions

1. Detection of metallo-beta-lactamases

The lack of detection of metallo-beta-lactamases in carbapenem resistant CF P. aeruginosa isolates is interesting but has little relevance for this paper.

The language needs attention.

In conclusion, I consider the data of interest but more information is necessary to be presented as well as possible explanations for these findings which seem different from data published in other CF centers.

Level of interest: An article whose findings are important to those with closely
related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interest below.