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Title: Side effects of tacrolimus upon airway epithelial tissue

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Body: In recent years, tacrolimus has become the most widely used immunosuppressive drug by lung transplant patients. However, tacrolimus is not free of side effects upon cells other than those from immunological system. We hypothesized that tacrolimus could affect airway mucociliary clearance, an important defense mechanism of respiratory tract against infectious agents. Twenty Wistar rats were equally divided into two groups to receive either saline solution (Control) or tacrolimus (TAC, 1 mg/kg/day). After 30 days of therapy by gavage, animals were killed and in situ mucociliary transport velocity (MCTV), ciliary beating frequency (CBF) and mucus production were measured. All TAC-treated animals showed a significant decrease in MCTV (1.54±0.42 and 0.79±0.32 mm/min, Control and TAC, respectively; p<0.001) and CBF (14.25±1.29 and 11.99±1.77 Hz, Control and TAC, respectively; p<0.001). However, there was no difference between groups concerning mucus production from airway goblet cells (5.48±1.76 and 5.57±1.14 %, Control and TAC, respectively; p>0.05). These data show that TAC plays an important role on the impairment of the mucociliary clearance which can be related with the high level of respiratory infections observed between 1 and 12 month after lung transplantation. This study was support by Sao Paulo Research Foundation-Fapesp.