Identification of pulmonary Oct-4+ stem/progenitor cells and demonstration of their susceptibility to SARS coronavirus (SARS-CoV) infection in vitro.

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摘要.

In this study, we report a serum-free culture system for primary neonatal pulmonary cells that can support the growth of octamer-binding transcription factor 4+ (Oct-4+) epithelial colonies with a surrounding mesenchymal stroma. In addition to Oct-4, these cells also express other stem cell markers such as stage-specific embryonic antigen 1 (SSEA-1), stem cell antigen 1 (Sca-1), and Clara cell secretion protein (CCSP) but not c-Kit, CD34, and p63, indicating that they represent a subpopulation of Clara cells that have been implicated as lung stem/progenitor cells in lung injury models. These colony cells can be kept for weeks in primary cultures and undergo terminal differentiation to alveolar type-2- and type-1-like pneumocytes sequentially when removed from the stroma. In addition, we have demonstrated the presence of Oct-4+ long-term BrdU label-retaining cells at the bronchoalveolar junction of neonatal lung, providing a link between the Oct-4+ cells in vivo and in vitro and strengthening their identity as putative neonatal lung stem/progenitor cells. Lastly, these Oct-4+ epithelial colony cells, which also express angiotensin-converting enzyme 2, are the target cells for severe acute respiratory syndrome coronavirus infection in primary cultures and support active virus replication leading to their own destruction. These observations imply the possible involvement of lung stem/progenitor cells, in addition to pneumocytes, in severe acute respiratory syndrome coronavirus infection, accounting for the continued deterioration of lung tissues and apparent loss of capacity for lung repair.

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