SV40T reprograms Schwann cells into stem-like cells that can re-differentiate into terminal nerve cells.

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**DOI:**
10.21203/rs.2.24550/v1

**SUBJECT AREAS**
Stem Cell & Developmental Cell Biology

**KEYWORDS**
Schwann cells, SV40T, cell transformation, cell reprogramming, Inverse differentiation, neurocrest cells
Abstract
Background: The effects of Simian virus 40 T antigen (SV40T) on various kinds of cells are different. Previous researchers failed to use SV40T immortalized nerve cells. However, they argued that SV40T caused nerve cell transformation. No one further study what is the specific effect of SV40T on nerve cells. We transfected Schwann cells (SCs) that did not have differentiation ability with MPH 86 plasmid containing SV40T in order to explore the effects of SV40T on Schwann cells.

Methods: SCs were transfected with MPH 86 plasmid carrying the SV40T gene and cultured in different media, as well as co-cultured with neural stem cells (NSCs). In our study, SCs overexpressing SV40T were defined as SV40T-SCs. The proliferation of these cells was detected by WST-1, and the expression of different biomarkers was analyzed by qPCR and immunohistochemistry.

Results: SV40T induced the characteristics of NSCs, such as the ability to grow in suspension, form spheroid colonies and proliferate rapidly, in the SCs, which were reversed by knocking out SV40T by the Flip-adenovirus. In addition, SV40T up-regulated the neurocrest markers Nestin, Pax3 and Slug, and down-regulated S100b as well as the late differentiation markers MBP, GFAP and Olig1/2. These cells also expressed NSC markers like Nestin, SOX2, CD133 and SSEA-1, as well as early development markers of embryonic stem cells (ESCs) like BMP4, C-myc, OCT4 and Gbx2. Co-culturing with NSCs induced differentiation of the SV40T-SCs into neuronal and glial cells.

Conclusions: SV40T reprograms Schwann cells to stem-like cells at the stage of neural crest cells that can differentiate to terminal nerve cells. Background: The effects of Simian virus 40 T antigen (SV40T) on various kinds of cells are different. Previous researchers failed to use SV40T immortalized nerve cells. However, they argued that SV40T caused nerve cell transformation. No one further study what is the specific effect of SV40T on nerve cells.

Full Text
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However, the manuscript can be downloaded and accessed as a PDF.

Figures
The SCs were transfected with SV40T and exhibited higher proliferative activity than that of primary SCs. Representative images showing (A) MPH86 plasmid structure, (B) Expression of SV40T in SCs, SV40T-SCs and cells in the Ad-Flip and Ad-GFP groups, (C) Cells in the Ad-Flip and Ad-GFP groups were stained with crystal violet at the indicated time points, (D) Percentage of proliferating cells in the Ad-Flip and Ad-GFP groups.
SV40T-SCs grow with stem cell-like growth characteristics. Representative images showing (A) primary SCs forming long synapses in NSC medium (magnification 100x), (B) adherent growth of SV40T-SCs with short synapses in complete DMEM (magnification 200x), (C) spherical colonies of SV40T-SCs in suspension in complete DMEM (magnification 200x), (D) a round shape, and formed spherical colony of SV40T-SCs in suspension (magnification 400x), (E) round shape, and formed spherical colonies of SV40T-SCs grown in suspension in NSC medium (magnification 200x), and (F) NSCs grown in suspension in NSC medium (magnification 200x).
The expression level of the neural crest markers and the NSC marker in SV40T-SCs. SV40T-SCs highly expressed Nestin, Slug and Pax3.

Figure 4

SV40T-SCs expressed markers of early neural differentiation. Representative images showing expression of Nestin (A), SOX2 (B), CD133 (C), SSEA-1 (D), BMP4 (E), C-MYC (F), OCT4 (G), and Gbx2 (H) (magnification 200x).
SV40T-SCs differentiated to neuronal and glial cells in the presence of NSCs. Representative images showing (A) RFP-labeled SV40T-SCs in complete DMEM (magnification 100x), (B) GFP-labeled NSCs and in complete DMEM (magnification 100x), (C) co-cultured SV40T-SCs and NSCs on day 1 (magnification 100x), (D-G) RFP-labeled SV40T-SCs on days 1 (D), 3 (E), 5 (F) and 7 (G) of co-culture with NSCs (magnification 200x), (H) GFP-labeled NSCs on day 7 of co-culture with SV40T-SCs (magnification 400x), and (I) the merging of G and I showed intertwined synapses of SV40T-SCs and NSCs on day 7 of co-culture (magnification 400x).

NSCs co-culture induces neuronal differentiation in SV40T-SCs. Representative images showing expression levels of (A) Nestin (magnification 100x), (B) β-III tubulin (magnification 400x), and (C) S100b (magnification 400x) in the co-cultured SV40T-SCs.
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