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Sven Ansorge

National Research Council, Canada

Aziza Manceur

National Research Council, Canada

Stéphane Lanthier

National Research Council, Canada

Sonia Tremblay

National Research Council, Canada

Anne-Marie Gélinas

National Research Council, Canada

See next page for additional authors

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Authors

Sven Ansorge, Aziza Manceur, Stéphane Lanthier, Sonia Tremblay, Anne-Marie Gélinas, July Dorion-Thibaudeau, Sophie Broussau, Julia Transfiguracion, Hafida Aomari, and Régnald Gilbert

Scalable Lentiviral Vector Production Using Stable Producer Cell Lines in Perfusion Mode

Sven Ansorge, PhD

National Research Council, Human Health Therapeutics Research Centre

May 6th, 2018

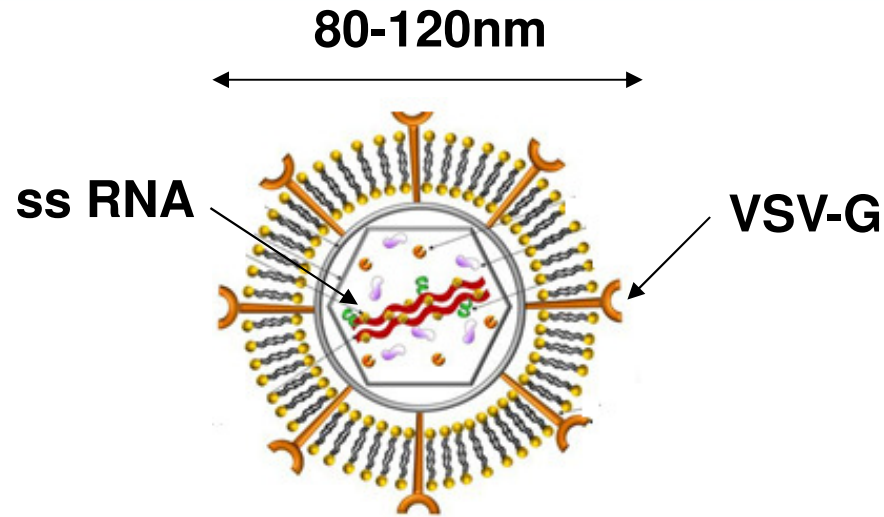


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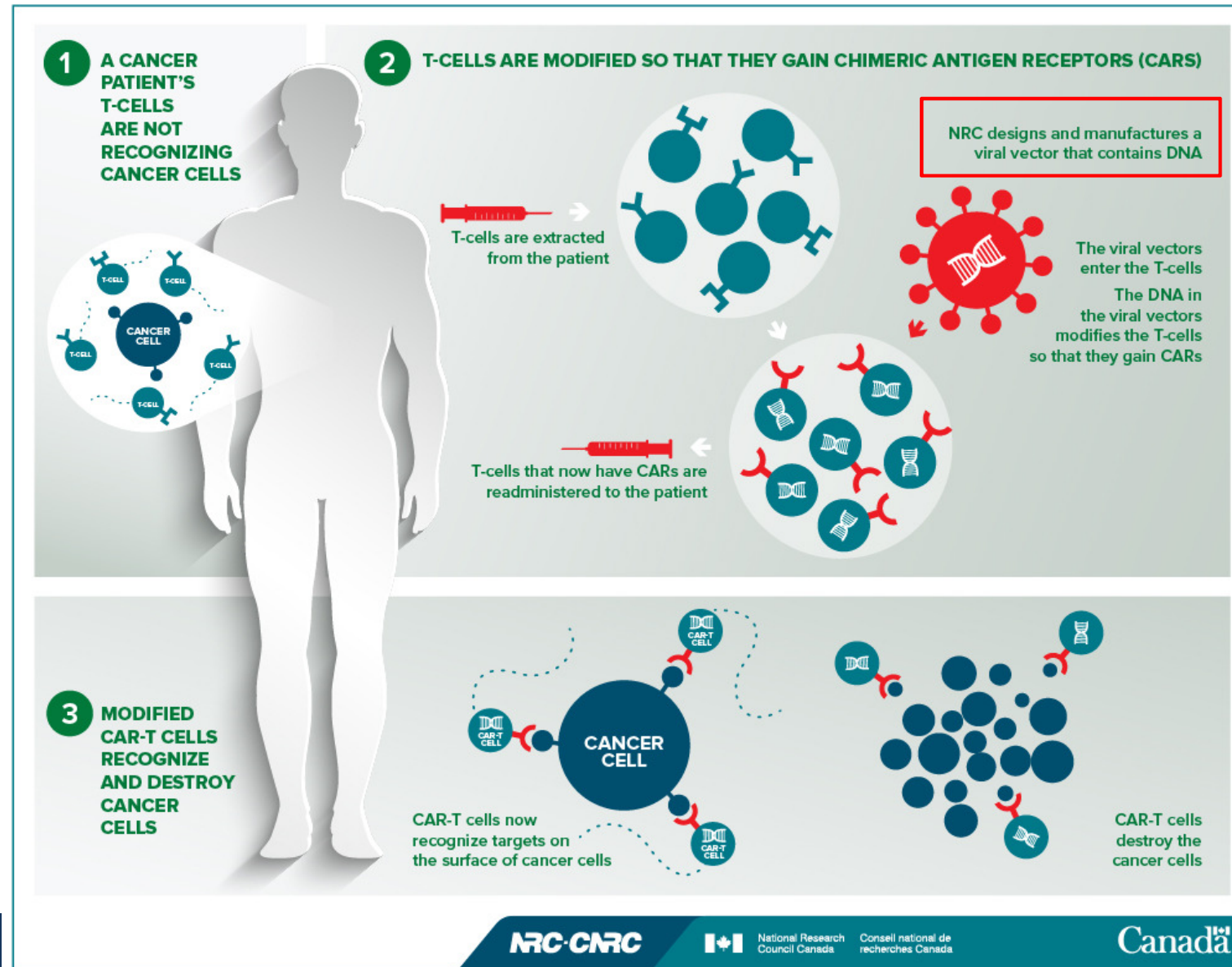
Canada 

Lentiviral vectors (LV) are used for gene and cell therapy



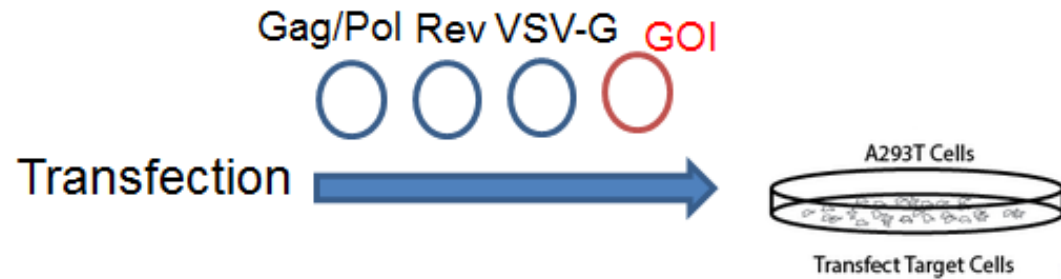
- HIV-based, enveloped virus
- Fragile, sensitive to pH and temperature
- Stable gene integration into genome of dividing and non-dividing cells

→ Gene therapy, CAR-T

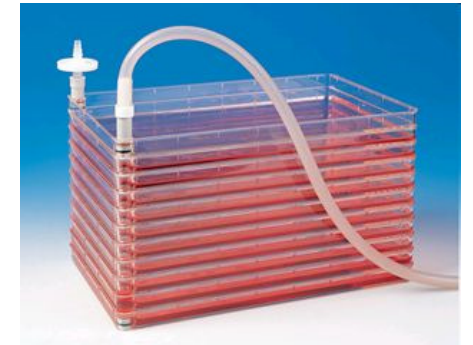


Bioprocessing of Lentiviral vectors (LV)

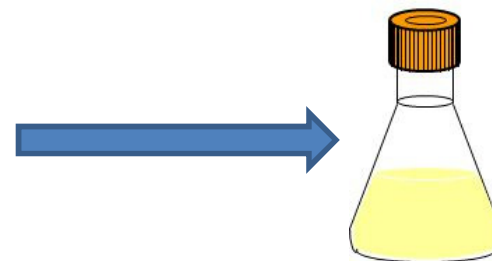
- Currently, LV are mainly produced in adherent cells by transfection of 4 plasmids: Virus accessory genes (Gag/Pol, Rev and VSV-G) and the gene of interest.



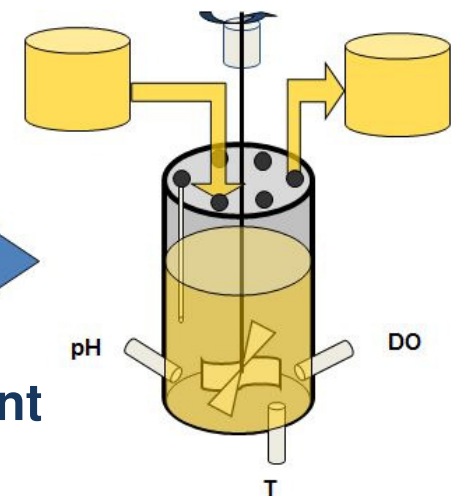
Issue with scalability



Objective: PD for stable producer cell lines (production of LV under the control of two switches) in suspension



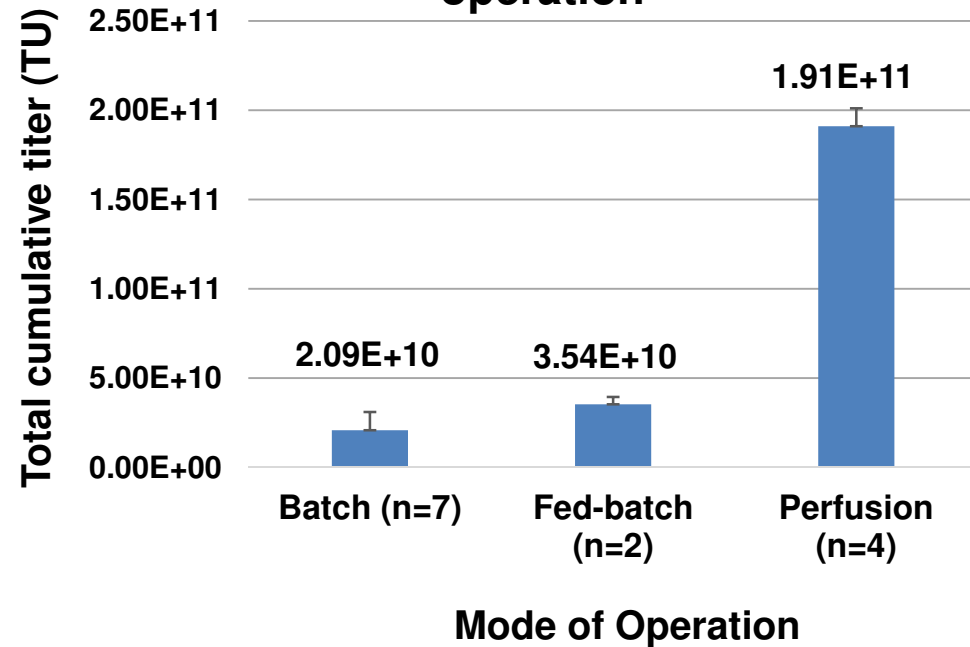
Process development



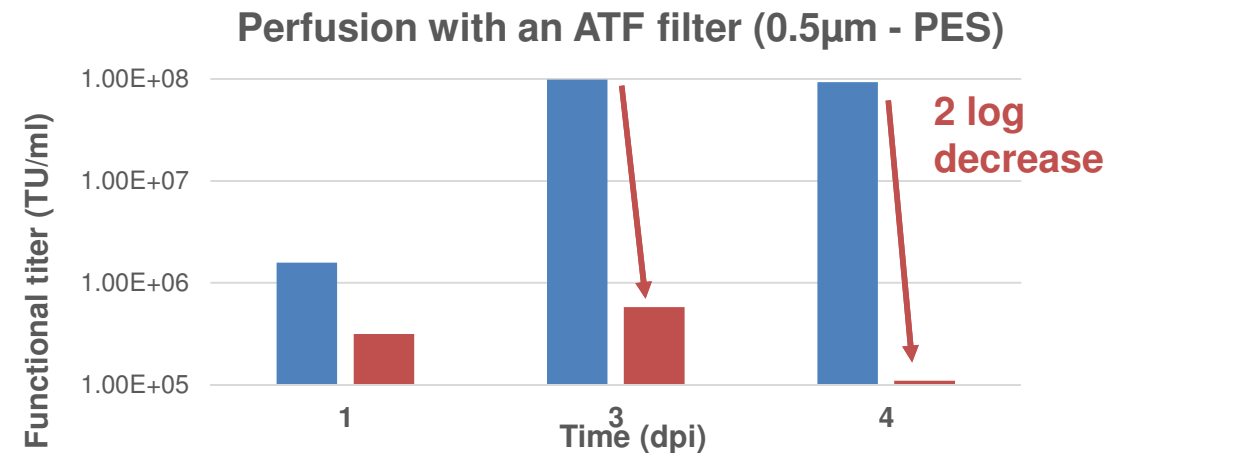
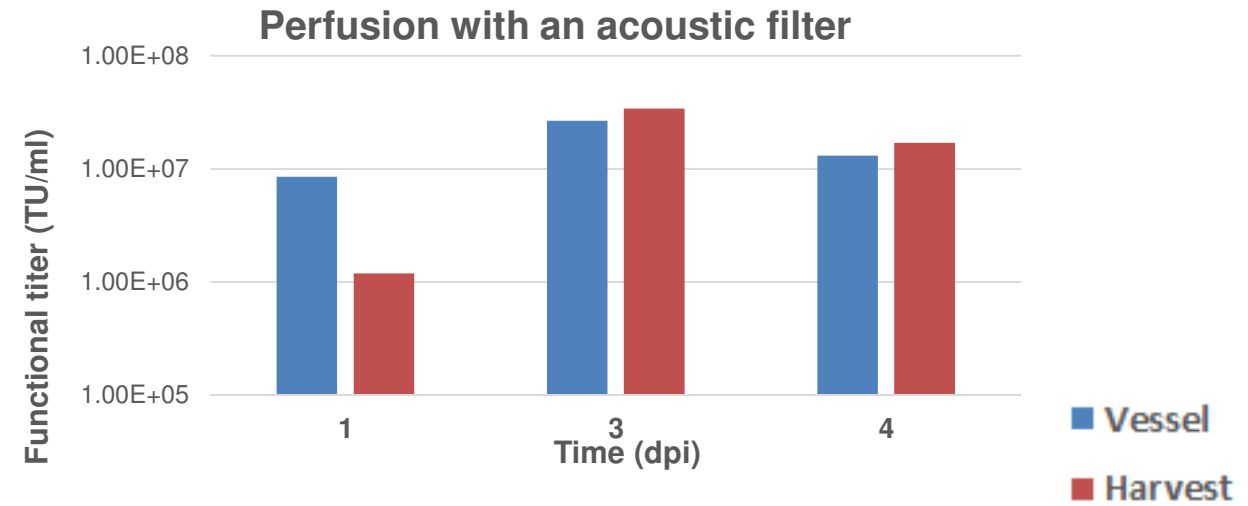
LV titers obtained under different modes of operation

Perfusion: Comparison of different cell retention systems

Total Yield with different modes of operation



10-fold yield increase when operating in perfusion mode (sequential harvests):
Manceur et al, Human gene Therapy, 2017



→ No sequential harvesting with ATF

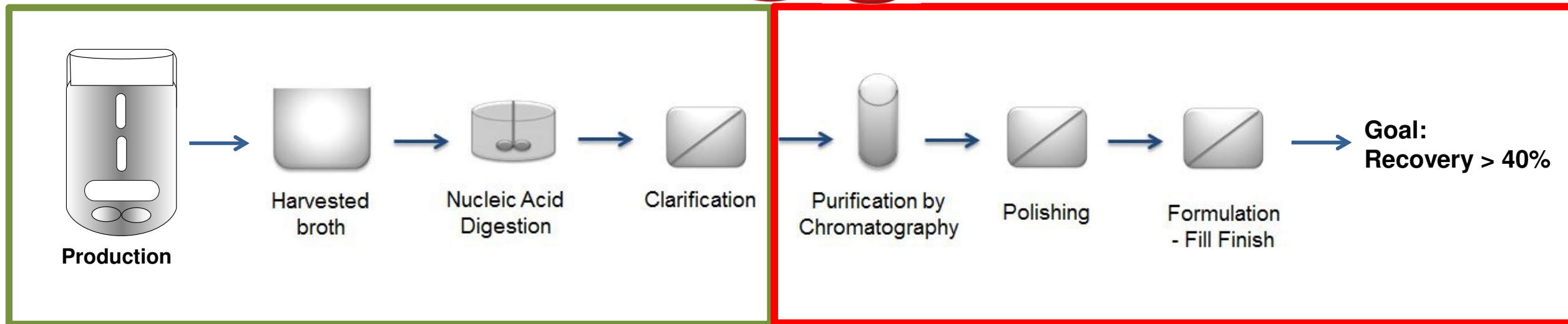
LV production and purification: towards 'continuous' bioprocessing

1. Transfer to GMP
2. Cost analysis/optimization/LV stability
3. Integrate USP and DSP



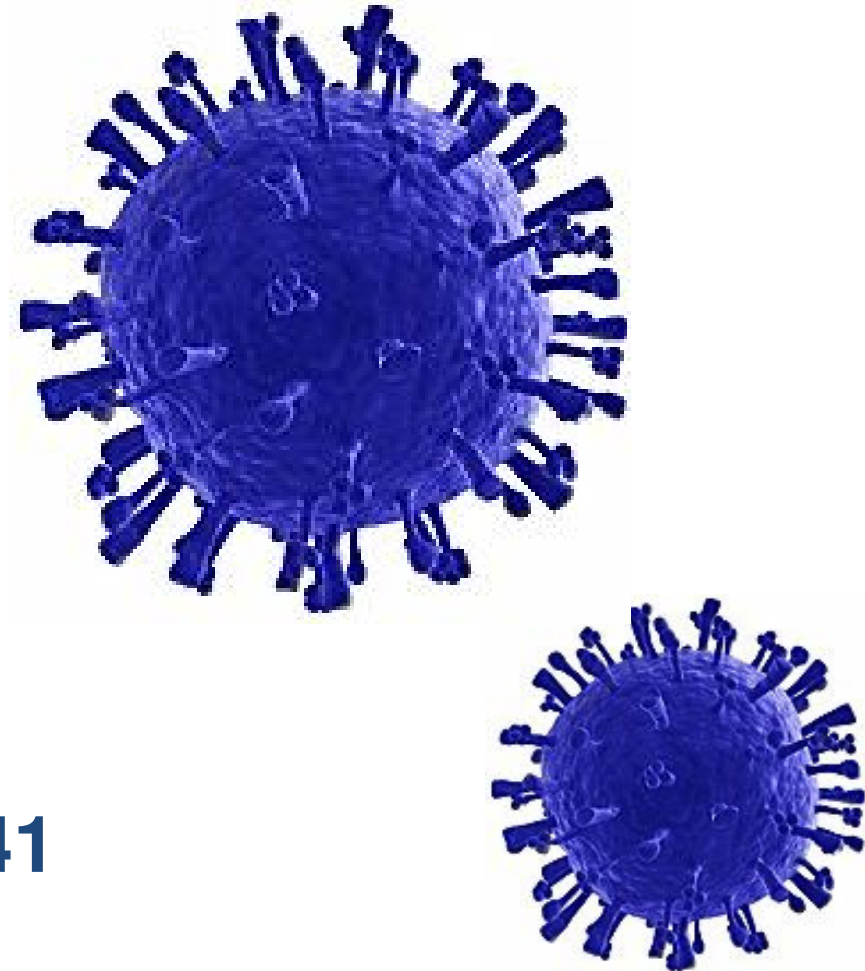
ready

under development



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- Sonia Tremblay
- Julia Transfiguration



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