Weill Cornell Medicine

Repurposing Atovaquone for Eliminating HIV-Infected T-Cells

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Background & Unmet Need

- Majority of patients with HIV are well-managed on chronic antiretroviral therapy (ART)
- Although ART suppresses HIV replication, it cannot eliminate integrated HIV within infected T cells, which creates a viral reservoir that triggers viral rebound if treatment stops
- Latency reversal agents (LRAs) intended to reactivate latent HIV have proven ineffective in reducing the viral reservoir despite enabling ART and immune recognition
- Persistence of HIV reservoirs are not only due to latency but also selection for infected cells that are resistant to killing
- **Unmet Need:** Therapy that effectively eliminates persistently infected HIV cells to achieve viral eradication

Technology Overview

- **The Technology:** Repurposing of Atovaquone (ATQ), as a treatment strategy for eliminating HIV viral reservoir
- **The Discovery:** HIV-infected CD4+ T-cells resistant to cytotoxic T-lymphocytes (CTL) have lower expression of gene-sets defining active metabolism and oxidative stress
- These cells have lower levels of intracellular ROS, making them more susceptible to agents that induce oxidative stress (e.g., ROS inducers)
- **PoC Data:** ATQ induces oxidative stress on human CD4+ T cells
- ATQ sensitizes infected CD4+ T-cells from multiple donors to CTL-mediated killing
- Currently evaluating effectiveness of ATQ in mouse models using patient-derive xenografts models of HIV infection

Inventors:
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Patents:
Provisional Filed

Publications:
N/A

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Technology Applications

- Complement existing ART, to clear HIV-positive T cells towards a functional or absolute "cure"
- Alone or in combination with other therapeutic agents, providing a new approach to managing HIV infections

Technology Advantages

- ATQ is an established and well-tolerated drug
- Serve a dual purpose, treating both latent reservoirs and protozoal infections in HIV patients
- Existing manufacturing processes and availability make ATQ a cost-effective option compared to newer, more specialized drugs

Supporting Data / Figures

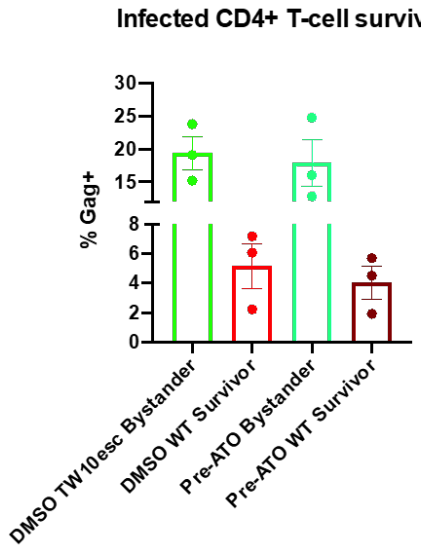

Figure 1: CD4+ T cells infected with wild-type HIV have a lower survival rate when pre-treated with ATQ (pre-ATO WT Survivor) compared to those that weren't (DMSO WT Survivor)

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