Microbiome-Derived Therapies for Treatment and Prevention Viral Infections

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Background & Unmet Need

- There are few antivirals for many viral infections including SARS-CoV-2, influenza, Zika, and CMV
- Limited access to antiretroviral therapy (ART) underlies most new HIV infections and HIV-related deaths
- Barriers to ART and other antivirals include toxicity, side effects, financial constraints, and lack of access to medical care
- There are few broad-spectrum antivirals, which would have the capacity to treat several different viruses
- **Unmet Need:** Development of novel antiviral strategies to overcome the lack of effective treatments, toxicity of current ARTs, and barriers to medicine for viral infections

Technology Overview

- **The Technology:** Methods of preventing viral infection, including HIV or CMV, using an aryl hydrocarbon receptor (AhR) agonist or Lachnospriaceae family bacteria
- **The Discovery:** Lachnospriaceae family members *Clostridium immunis* (*C. immunis*) and *Ruminococcus gnavus* (*R. gnavus*) metabolize tryptophan into 3-indolelactic acid (3-ILA) via Aromatic Amino Acid Aminotransferase (ArAT)
- 3-ILA and FICZ (an alternative agonist) can prevent HIV infection by binding to aryl hydrocarbon receptor (AhR)
- **PoC Data:** Administration of *C. immunis* as a live biotherapeutic suppresses active HIV replication by up to 80-90% *in vitro* in an ArAT dependent manner
- Administration of FICZ suppresses active HIV replication by up to 50% *in vitro*

Inventors:
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Patents:
Provisional Filed

Publications:
N/A

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Cornell Reference:
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ART: Antiretroviral therapy
AhR: Aryl hydrocarbon receptor
ArAT: Aromatic Amino Acid Aminotransferase
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| Use of small molecule AhR agonists or *Lachnospriaceae* live biotherapeutics to prevent HIV infection in infants who breast-feed from HIV-positive mothers | \[
\begin{align*}
\text{C. immunis} & \rightarrow \text{ArAT} \\
\text{3-ILA} & \\
\text{Ahr} & \uparrow \text{FICZ} \\
& \downarrow \text{HIV}
\end{align*}
\]

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| AhR agonists or *Lachnospriaceae* bacteria are broad-spectrum and can be used for co-infections | \[
\text{ART} \quad \text{FICZ}
\]
| Prolonged colonization of *Lachnospriaceae* in patients can prevent the need for re-dosing | \[
\text{AhR} \quad \text{Ahr} \quad \text{HIV}
\]
| AhR agonists or *Lachnospriaceae* can be used as a monotherapy, rather than in combination like ARTs | \[
\text{3-ILA} \quad \text{AhR} \quad \text{FICZ}
\]
| May overcome the toxicity of current ART regimens | \[
\text{HIV} \quad \text{Ahr} \quad \text{FICZ}
\]

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**Figure 1:** Schematic of HIV inhibition by *C. immunis*. *C. immunis* prevents HIV infection by expressing ArAT, which produces, 3-ILA, which activates Ahr.

**ART:** Antiretroviral therapy
**AhR:** Aryl hydrocarbon receptor
**ArAT:** Aromatic Amino Acid Aminotransferase
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### Supporting Data / Figures

**Figure 1:** a) *C. immunis* prevents HIV infection in an ArAT-dependent manner. b) 3-ILA alone can prevent HIV infection c) aryl hydrocarbon receptor (3-ILA target) agonist, FICZ can prevent HIV infection.

**Legend:**
- WT: Wild Type
- ΔArAT: ArAT Knockout
- DMSO: Dimethyl Sulfoxide
- 3-ILA: 3-Iodoindole Acetate
- FICZ: 3-ILA agonist

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