Inducing Immune Quiescence

Grand Challenge Canada

Stars in Global Health (Round 5)

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Outline

- The research
  - Where it is coming from
  - Our bold idea
  - Update of the project

- Tips for success
To know about GCC Star in Global Health

- 100,000$ for 12 to 18 months
- Proof of concept
- Collaboration with a low-middle income country

Kenya
HIV: Global Health Problem

- Two-third of new infection by HIV affects women (1.2 millions of new infection per year).

- In Africa, women are twice likely to be infected by HIV during unprotected vaginal intercourse compared to men.

- In Kenya there are over 27,000 sex workers and despite prevention efforts, HIV incidence remains really high in this vulnerable population, which serves as catalysts for HIV transmission to the community.

- Important need for a new preventive method that would empower women to protect themselves.
Background behind our Bold Idea
T cell Immune Quiescence hypothesis

- Decreased levels of baseline T cell activation and higher level of Treg limit the number of HIV target cells at the genital tract.
Our bold idea

The Immune Quiescence phenotype observed in HESN women can be mimic to decrease the potential number of HIV target cells at the female genital tract and prevent HIV infection.
Why our bold idea is innovative?

- Modulating the lymphocyte activation at the genital tract could represent an NEW AVENUE in the fight against HIV infection.

- PrEP too expensive for large scale
- Vaccine/microbicide not available yet
- If a vaccine/microbicide is available in the next 5-7 years, efficiency is not 100%; therefore, the new preventive method could be used with this
How to Induce Immune Quiescence and trying to make it accessible to everybody

- Anti-inflammatories:
  - Decrease inflammation
  - Decrease immune activation

- Selection of two anti-inflammatories
  - Hydroxychloroquine (HCQ) (brand name: Plaquenil) (200mg/daily)
  - Acetylsalicylic acid (A.A) *brand name: Aspirin (81mg/daily)
Why the selection of these two drugs?

**HCQ:**
- Anti-malaria drugs
- Use for the treatment of autoimmune disease such as rheumatoid arthritis and lupus
- In vitro anti-HIV activity (Sperber et al., AIDS RES HUM RETROVIRUS 1993)
- Debate on its efficacy on HIV disease progression (Piconi et al., Blood 2011; Paton et al, JAMA 2012)

**A.A:**
- Over the counter anti-inflammatory
- Use in long-term for heart disease prevention
- Showed to decrease inflammation in HIV infected individuals and help with disease progression outcome (Burkholder et al Clin infect dis 2012)

- Both drugs are affordable, widely available, safe, no stigma
Participants

- HIV negative low risk women

- 80 total

- After randomization:
  - 40 will be on HCQ
  - 40 on A.A.
How will the study being conducted?

Analysis of the immune activation in women taken aspirin or HCQ

<table>
<thead>
<tr>
<th>Pre-screening</th>
<th>Visit 1</th>
<th>Start of drug treatment</th>
<th>Visit 2: women are taken daily HCQ (200mg) or aspirin (75mg), since 2 weeks.</th>
<th>Visit 3: women are taken daily HCQ (200mg) or aspirin (75mg), since 6 weeks.</th>
<th>Follow up visit assessing for side effects</th>
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At visit 1, 2 and 3, blood, CMCs and CVL will be taken.
The first step of IIQ study... assessment of feasibility

- In November 2013, we held a focus group to reach HIV negative low-risk women.

- Relative of clients attending Baba Dogo and Pumwani clinic were reached. (both clinics are working with HIV+ clients)

- 80 participants came to the meeting and another 20 asked to assist and were put on a waiting list. Majority of women in couple came with their husband or boyfriend.
Community engagement

- Focus group helped us to bring the community on board

- Focus group + pre-screening: offers the possibility for women to get HIV tested and if HIV+ be enrolled in one of our program to receive free care

- Boyfriend/Husband engagement in the study.
From Oct 2013-oct 2014

- Sign contract with GCC
- Got Ethic approval from UofM and UofN
- Build team
- Pre-screening
- Enrolment and study

Prior getting GCC:
- Discussed with our international collaborator about feasibility
- Started building protocol and documentation
Where is the study now?

- Recruitment is done

- 16 participants terminated the whole study mid-September

- By last week of November all participants will have completed the study visits.

- Preliminary analysis is starting on the participants who terminated the study
  
  - Looking at T cells CD4+ activation status (CCR5+, CD69+) in female genital tract and blood.

- According to results, we are planning to apply to the transition scale in the winter 2015

- Link with industry and government
Before applying to GCC

- Have a strong BOLD IDEA. Needs to be innovative and addressing an important public health issue
  - The most important point from the reviewers of CIHR was the innovation behind our idea

- Have a good mentor
  - Dr Allan Ronald and Dr Keith Fowke
  - Reviewer Comment: Young PI but supported by a strong team
Before applying to GCC

- International team
  - To apply to the Stars in Global Health program you MUST have to link with a low/middle country.
  - This takes time. You need to have your collaboration in place prior applying (not enough time to do so once you have the grant)
  - Have a strong and trained team

IIQ team during a training session
International collaboration

- Advantage of building on collaboration already existing
- UofN/UofM have a strong collaboration
  - Collaboration already in place since 30 years
  - Contract between the two Universities already in place
  - I had the support from the team
  - Prior applying I had discussed with the community about interest.
- Needed a trained team
When applying

Proposal

Really limited space you have to say everything you would like to say. GCC have a specific form to be filled out. You have to answer to each question and the space (word count) is really small.

- Be focussed
- Go directly to the point
- Right at the first question make the point about the important of the problem you would like to address and how UNIQUE is your approach. Show you are special and only you could do it
- Have straight forward measurable outcomes
When applying

- Video!!
  - Explaining all the background, idea and study in two minutes!
  - Budget enough time for this!
    - Review as many of winning video as you can
    - Need to be understandable for all... don’t be too technical
    - Make sure your bold idea is clear
    - Ensure that the sound and your voice is clear
    - If the video includes other people than yourself make sure you have an written authorization

My video:
- We used my camera to make the video. In house video (filming and editing). No cost associate with it
- iMovie is a friendly user and really useful tool!
While awaiting for the decision

- Connect with people to go voting for your video
  - Facebook/Twitter
  - Friends of friends
  - Department

- Show you can reach the general population and they are interest in your idea (Our video ended in the top 10)
- The link with the population is important for GCC so show you’ll be able to do knowledge translation and reach the general population
Once you get it

- Contract signature: Takes time and can be quite complicated
- They want results in a short period of time so you need to be ready if you get it to start almost right away
  - Not the time to build international collaboration
  - Have your ethics done if needed
  - Team trained
- Start as soon as you can
Be ready

- You never know what can happen... Be prepare
- Have a plan B, C, D...
  - More than one site: Other clinics to do recruitment
  - Build a team that could moved

- If you are not used to social media starts now!
If I was starting over

- Ethic approval prior knowing if we get the grant or not
- Be more involved in social media
Sometimes you bring more to the community than what you thought the project was about

- HIV testing
- STIs testing
- Education
- Free Health care
- Capacity building
Important to have

- Community engagement
- Co-investigator in a low-middle income country
- Good mentor (for people who are not PI)
- Innovative idea that could have a global health impact
- Strong partnership with the low-middle income country
Thank you....

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- Lucy Mwamgi, Ken Odunor, Domnic Ouma

ALL PARTICIPANTS