

Off-Target effects of
vaccination
An Industry perspective

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Disclaimer

- This presentation is intended to present some of my own considerations
- It does not represent a collegial, agreed upon, Industry perspective



THE MILLENNIUM DEVELOPMENT GOALS (MDGs) ARE THE MOST SUCCESSFUL GLOBAL ANTI-POVERTY PUSH IN HISTORY. LET'S STEP UP ACTION TO THE 2015 MDG TARGET DATE AND BEYOND.

MDG4



REDUCE CHILD MORTALITY

17,000 FEWER

CHILDREN DIE EACH DAY THAN IN 1990

LET'S STEP UP

6 MILLION+ CHILDREN STILL DIE

BEFORE THEIR FIFTH BIRTHDAY EACH YEAR

Awareness

- Initial observations published 20+ years ago
- WHO looking at the evidences since early 2000's
- Awareness remains low in both academic and industrial circles
- A counter intuitive concept for vaccine developers
- Previous gatherings have not led to action
- Significant industry representation (high income countries) at this meeting

NSEs : sorting things out

- Trained Immunity
 - Adaptive component of innate immunity
 - Innate Like B cells
- Cross reactivity
- Ancillary effects

NSEs : sorting things out

- Trained Immunity
 - BCG as “prototype”
 - Unlikely to be deleterious
- Cross reactivity
 - Can be good or bad
- Ancillary effects
 - Non Infectious Diseases
 - Measles?

BCG: an unique situation

- Consensus on the positive effects
- Initial mechanistic rationale
 - Innate immune memory
 - Epigenetic reprogramming
- Recognized variability between (also within?) vaccines
- Unique situation of use in both TB prophylaxis and cancer immunotherapy
- Waste avoidance and other pragmatic considerations lead to suboptimal timing of administration

BCG: “quick” win?

- Compare strains in Systems Vaccinology studies
 - Hope to identify critical differences
- Look for signatures in the field
- Further “Mode of Action” studies
- Once identified, critical feature(s) allow to optimize and standardize process and strain
- Develop single dose presentation
- Recognize value and pay for it!

Measles

- Moves from NSE to SE (prevention of immunomodulation)?
 - Will help uptake?
- Mostly old fashioned manufacturing methodology. One MNC has communicated that it will stop production
- Promote value

DTP

- Intuitively one considers pertussis, but there is also D and T in there
- Not a “clean” vaccine and lots of variability
- Run the proposed “booster” trial, assuming it can be properly designed

An off-target effect we spoke little about

- Immunotherapy is hot field in oncology
- BCG in urology since the 90's
- Recent observations using other conventional vaccines

Tetanus toxoid and CCL3 improve dendritic cell vaccines in mice and glioblastoma patients

Duane A. Mitchell^{1,2,3*}, Kristen A. Batch^{2,3*}, Michael D. Gunn^{4,5}, Min-Nung Huang⁵, Luis Sanchez-Perez², Smita K. Nair⁶, Kendra L. Congdon², Elizabeth A. Reap², Gary E. Archer^{1,2}, Annick Desjardins^{1,2}, Allan H. Friedman^{1,2}, Henry S. Friedman^{1,2}, James E. Herndon II⁷, April Coan⁷, Roger E. McLendon^{1,3}, David A. Reardon^{1,2}, James J. Vredenburgh^{1,2}, Darell D. Bigner^{1,2,3} & John H. Sampson^{1,2,3,5,8}

UCSF-Led Study Explains How Early Childhood Vaccination Reduces Leukemia Risk

Chronic Infections Push 'Pre-Leukemia' Cells, Common in Newborns, into Malignancy

By [Juliana Bunim](#) on May 18, 2015 | [Email](#) | [Print](#)



An off-target effect we spoke little about

- Immunotherapy is hot field in oncology
- BCG in urology
- Recent observations using other conventional vaccines
- **A driver to raise general awareness of Vaccine NSEs?**

What needs to happen?

- Understanding of the Mode of Action
- Run RCTs
 - Standardize methodologies
- Get the NS indication on the label!
 - Get the data
 - File
 - Regulatory approval
 - How to get WHO Prequalification?
- Get Recommendation
- Not trivial and not fast

How to strengthen the case?

- Mechanistic studies
 - In vivo, in vitro, in silico
- RCT when feasible
- Controlled Human Infection Models?
 - Recent increase of activity in this field
- Animal Models
 - Human pathogens and animal

Who pays?

- Precompetitive funding mechanisms
 - IMI, EDCTP
- NIH
- Donors
 - BMGF, Governments, others
- Industry contribution
- Other?

Next steps

- Address topic as a community
 - Champions
 - Sceptics
 - Academics
 - Industry
 - Regulators
 - Donors
 - ...
- Prioritize
 - Among vaccines
 - -Among questions
- Concrete steps tbd this afternoon

Thank You