WORLD ANTI-DOPING AGENCY

WADA Perspectives on Gene Doping in Sport

Dr. Olivier Rabin

Science Director

WADA

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Evolution of analytical methods

- Anti-doping analyses started in the 60s based upon detection of drugs in urine (Stimulants & Anabolic Steroids).
- Progressive incorporation of :
  - Immunoassays:hCG (1987); LH (1997); hGH(2004).
  - Electrophoresis / focusing: EPO (2000); HBOCs (2004).
  - Flow cytometry: blood transfusions in 2004.

  Trend evolving from pure chemical analysis to incorporate more biochemistry and biology.

Evolution of rules

- From imperative need to detect and characterize the doping substance(s) in athlete's biological specimen.

to

- Possibility to use markers of abuse of substance(s) to report doping.

As long as scientifically validated (concept and methodology)…

- Markers approach already in final development phase for hGH detection:
  - IGF-1(liver)
  - P-III-P (bone)
- Abnormal markers variations are used to qualify doping.
- However, almost 10 years of research and more than 4 M$.

Fundamental Concept

- Abuse: substance extra gene

Non physiological modification
(imbalance)

- Detection:

Where to look?

Genomic

Transcriptomic

Proteomic

Metabonomic

- What to look for?
  - Signature(s) of changes unique to doping class(es) of substance(s).

  Limits in:

  - Interpretation of gene modifications.
  - Protein and peptide knowledge.
  - Interpretation of metabolic changes.
- Where to look for?
  - Accessible cells or biological fluids with minimal invasiveness (urine?? blood cell lines, buccal cells,…).
  - Imaging (changes, markers, radiolabeled tracers)

Challenges faced

- Identification or right target(s): Where, what, how (interpretation).
- Accessibility to measurable modifications (invasiveness, time window, ethical methods).
- Eliminate other explanations than doping (gender, age, diseases, environment, ethnicity,...).
- Development of specific tools for anti-doping.

Challenges faced (II)

- Extremely sophisticated gene constructs with fine modulation already in animal models.
- Approaches may well work for gene doping or some substances, but what about cell therapy, in particular autologous cell transplants?
- Costs.
- Layman accessible!

Hope…

- EPO study in monkey showed genetically transferred EPO still detectable.
- Microarrays and SAGE appear to reveal target genes or mRNA. Proteins are promising. Metabonomics will grow.
- Combination of discriminant factors.

Pragmatism…

- Science is likely to deliver the antidote. When and how?
- Resources can be very demanding on antidoping, and beyond capability. Need to partner.
- Hope for some large scope methods, not too narrow in application.
- Even if gene doping applied, limited chances of success, delay in significant impact in sport, though success will come…

Contact

HEADQUARTERS

Stock Exchange Tower
800 Place Victoria, Suite 1700
Montreal, Quebec H4Z 1B7
CANADA

Tel. : +1 514 904 9232
Fax : +1 514 904 8650
info@wada-ama.org

www.wada-ama.org

REGIONAL OFFICES

Europe
Avenue du Tribunal-Fédéral 34
1005 Lausanne SWITZERLAND
Tel.: +41 21 343 43 40
Fax: +41 21 343 43 41

Asia/Oceania
c/o Japan Institute of Sports Sciences
3-15-1 Nishigaoka, Kita-Ku
Tokyo, 115-0056 JAPAN
Tel: +81-3-5963-4321
Fax: +81-3-5963-4320

Africa
Protea Assurance Building, 8th Floor
Greenmarket Square
Cape Town, 8001 SOUTH AFRICA
Tel: +27 21 483 9790
Fax: +27 21 483 9791

Latin America
Montevideo URUGUAY
Opening late 2005

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