

WADA Perspectives on Gene Doping in Sport

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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 of 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...

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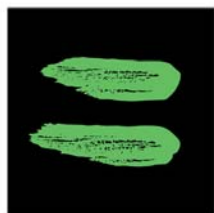
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