

# WADA Research Program on Gene Doping

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# 1<sup>st</sup> Gene Doping Symposium

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Banbury (New York – USA) March 2002

First meeting on Gene Doping. Established a multidisciplinary basis of Gene Doping concept

Recommendations:

- Dialogue & consultation around genetic technologies
- Insert Gene Doping on the Prohibited List
- Initiate research program under WADA auspices

# 1<sup>st</sup> Gene Doping Symposium

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Gene Doping defined for the first time in the 2003 IOC List of Prohibited Substances and Methods:

Section II Prohibited Methods – C. Gene Doping

*"Gene or cell doping is defined as the non-therapeutic use of genes, genetic elements and /or cells that have the capacity to enhance athletic performance"*

# 1<sup>st</sup> Gene Doping Symposium

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- Prohibition of Gene Doping in 2003 :

Allowed submission of research project grants applications under "*Compounds or methods enhancing growth*"

- Inserted as a priority theme in May 2004 as

*"Gene and cellular technologies applied to sports"*

# Initiation of Gene Doping Research

- Initial theme in 2004: *"Gene and cellular technologies applied to sports"*
- In 2006, *"Gene and cellular technologies of relevance to doping, i.e. detection of gene doping; identification of suitable cells for minimally invasive detection of gene-doping; detection and identification of patterns or global signatures associated with gene transfer or gene manipulation, including gene expression technologies, proteomics, metabolomics, immune signatures, transcriptomics; non-invasive imaging; detection of exogenous cell transfer/therapy"*

# Initiation of Gene Doping Research

In 2008, theme has evolved to:

*“Detection of Prohibited Substances/Methods: **novel methodologies**, i.e detection of gene doping and gene manipulation including patterns or global signatures associated with gene transfer (**vectors**, gene products, biological markers, non-invasive imaging); detection and identification of prohibited substances and methods and their biological signatures by molecular biology techniques, proteomics, transcriptomics, metabolomics, immune signatures; detection of exogenous cell transfer/therapy”*

# Development of Gene Doping Research

- In 2003: 3 projects only submitted from known research groups; 2 approved.

Then:

- 7 applications submitted & 2 retained in 2004
- 15 projects submitted & 4 approved in 2005
- 22 applications & 8 retained in 2006
- 19 projects submitted & 5 approved in 2007

Total of 66 projects submitted to WADA, 21 selected after independent review process and discussion at HM&R Committee meetings and approved by WADA Executive Committee.

# Gene Doping definitions

- Gene doping definition evolves in the WADA List of Prohibited Substances and Methods:

Defined in 2004 as *"The non-therapeutic use of cells, genes, genetic elements, or of the modulation of gene expression, having the capacity to enhance athletic performance, is prohibited"*

- Remained idem from 2005 to 2008
- Proposal for 2009: *"The transfer of cells or genetic elements or the use of cells, genetic elements or pharmacological agents to modulating expression of endogenous genes having the capacity to enhance athletic performance, is prohibited"*

Reflecting evolution of knowledge and adaptation to evolving science and discussion in the field.

# Gene Doping research in 2008

- Maturity in research program with 20 projects submitted currently under review from 25 research teams (25 principal investigators from 12 countries) around the world.
- Selection in September 2008 by HMR and approval by ExCo.
- Another portion of 6.5 M\$ will be distributed to gene doping projects and will join the already 7.8 M\$ committed by WADA to this research theme (25 % of the total 31.5 M\$ committed by WADA to Anti-Doping research).

# Research themes 2004-2007

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- 21 projects in the areas of
  - Genomic/Transcriptomic
  - Proteomic
  - Metabolomic
  - Viral detection
  - Bioinformatics

# Genomics/Transcriptomics

## ➤ Molecular signatures (I)

up or down regulations of genes, mRNA or proteins combined revealing changes specifically related to doping abuse.

- Growth Hormone

- ✓ Dr G. Gmeiner (Austria)
- ✓ Pr T. Friedmann (USA)
- ✓ Pr K. Ho (Australia)

- IGF-I

- ✓ Pr T. Friedmann (USA)
- ✓ Dr M. Giacca (Italy)
- ✓ Dr R. Holt (UK)

# Genomics/Transcriptomics

## ➤ Molecular signatures (II)

- Steroids
  - ✓ Dr M. Schönfelder (Germany)
- Erythropoietin/Hypoxia
  - ✓ Dr S. Imagawa (Japan)
  - ✓ Dr J. Rupert (Canada)
  - ✓ Dr S. Lahiri (USA)
- Autologous blood transfusion
  - ✓ Dr M. Ashenden (Australia)
  - ✓ Dr J. Rupert (Canada)
- Myostatin
  - ✓ Dr P. Diel (Germany)
  - ✓ Dr T. Khurana (USA)

# Genomics/Transcriptomics

## ➤ Detection methods

- Gene transfer
  - *In vivo* imaging
    - ✓ Dr J. Segura (Spain)
  - *In vitro* diagnostics
    - ✓ Drs R. Snyder & P. Moullier (USA/France)
    - ✓ Dr P. Simon (Germany)
- siRNA transfer
  - ✓ Dr J. Rupert (Canada)

# Proteomics

- Growth Hormone
  - ✓ Dr J. Roberts (UK)
  - ✓ Dr M. Thevis (Germany)
  - ✓ Dr J. Jorgensen (Denmark)
- IGF-I
  - ✓ Dr J. Roberts (UK)
  - ✓ Dr M. Giacca (Italy)
- Autologous blood transfusion
  - ✓ Dr J. Segura (Spain)

# Bioinformatics

- Establishment of a bioinformatics core facility at UCSD for the evaluation of research results of genomics and proteomics effects of doping agents.
  - ✓ Prof. T. Friedmann and Drs R. Bashker & S. Subramanian (USA)

# Reflection to maturity

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From initial experiments to pragmatism :

- ✓ Small amplitude of variations.
- ✓ Coherence of modulations observed vis-à-vis known mechanisms.
- ✓ Specificity of changes.
- ✓ Limit of knowledge and technologies.

# Now and future...

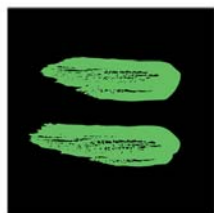
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- Consolidation phase of current experiments and results
- Other technologies to be considered:
  - Any other pathways to explore.
  - Issues of innovation versus robustness in anti-doping applications.

# Conclusions

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- ✓ Maturity of Gene Doping research theme achieved.
- ✓ Relatively promising return to date.
- ✓ Initial results indicate variable outcomes.
- ✓ Results need consolidation in near future.
- ✓ Specific development for anti-doping?
- ✓ Other areas to explore?



**WORLD  
ANTI-DOPING  
AGENCY**



**play true**