Coresta
Advanced Technologies Cambridge

10 november, 2011

Our Purpose

BRITISH AMERICAN TOBACCO

Using Biotechnology to Provide British American Tobacco with a Competitive Advantage

Continually exploring and implementing new to world Capabilities and Techniques

About Advanced Technologies Cambridge (ATC)

- Established as a Joint Venture between British American Tobacco Industries and Twyford Plant Laboratories in 1987

- Moved to the Cambridge Science Park in 1988
  - Centre of Excellence for plant science
  - Universities
  - Concentration of high tech companies

- Wholly owned subsidiary of British American Tobacco
  - In-house programmes
  - Commercial partnerships with third parties
  - Government funded collaborative projects

Advanced Technologies Cambridge

Monsanto Platform

British American Tobacco

Genomics
Genomics involves the mapping of the genes of plants to understand their structure and the role they play in how the plant functions.

Conventional breeding
Conventional breeding is the process of cross-pollinating plants with desirable qualities to develop improved plants in successive generations.

Molecular breeding
Molecular breeding involves the use of DNA markers for genes in combination with physical meas-urement of traits to manage plant breeding programs by shortening cycles. Molecular breeding significantly accelerates the efficiency in bringing new varieties.

Crop analytics
Crop analytics involves the application of advanced analytical methods and technologies to identify the comp-osition of food and feed traits.

Biotechnology
Biotechnology is the application of scientific knowledge to transfer beneficial genetic traits to enhance plants' growth or to provide nutritional or other benefits to farmers, food and feed processors, or consumers.

Animal productivity
Animal productivity uses the specific application of technology to improve the milk and meat production of livestock.

Pipeline Research – Development (seed Biotech model)

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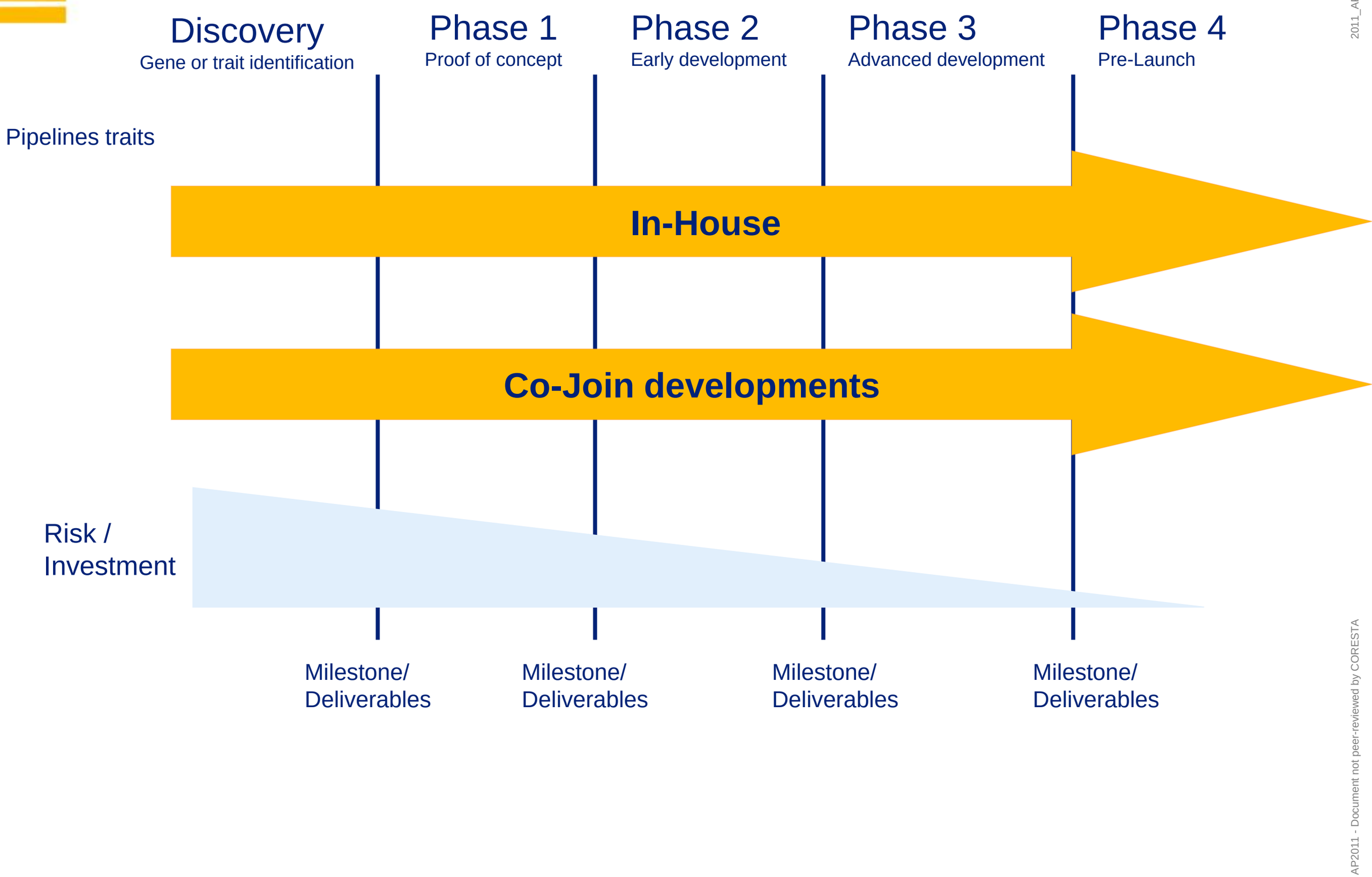


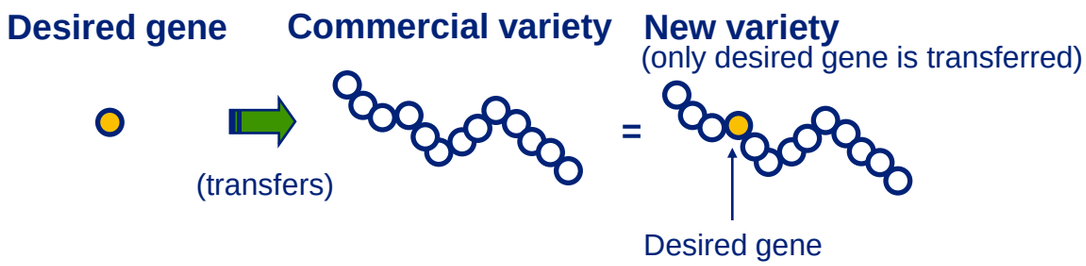
Research Approach

Targeted GM

Transgenic approach

GM

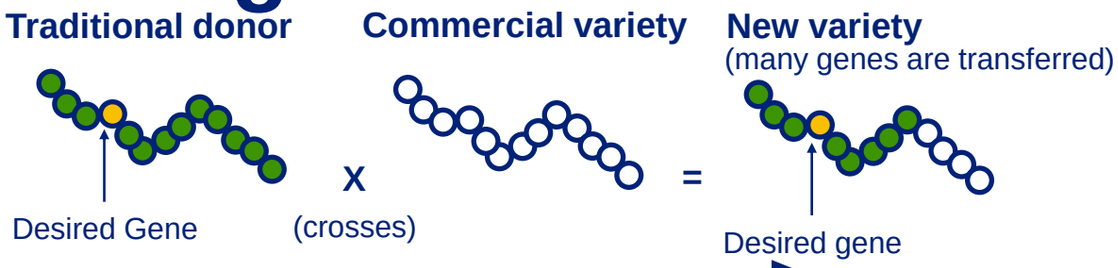
Using plant biotechnology, a single gene may be added to the strand.



High Throughput

Plant breeding-Non GM

DNA is a strand of genes, much like a strand of pearls. Traditional plant breeding combines many genes at once.



Natural variation

Molecular breeding approach

Open Innovations

Licensing
In & Out

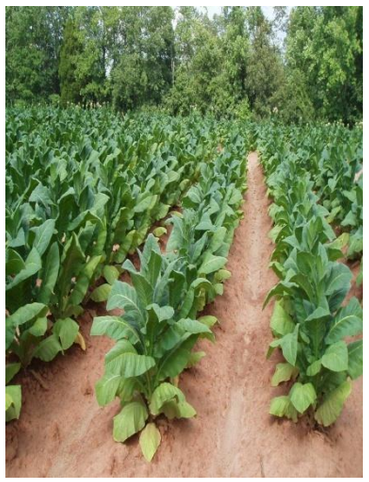
Collaborations

Partnerships

Universities

Advanced Technologies
Cambridge

Industry

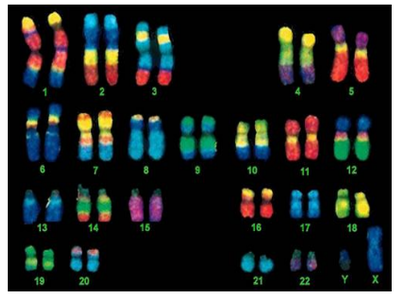


Research Areas

- Harm reduction strategies
  - Toxicant precursor reduction
  - Tobacco specific nitrosamines (TSNAs)

- Sustainability of tobacco agriculture
  - Reducing usage of crop protection chemicals

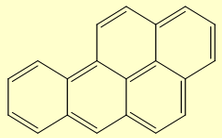
- Non-GM approach to tobacco issues
  - Utilising naturally occurring variation in tobacco genes
  - Understanding the tobacco genome to develop a state-of-the-art global breeding programme



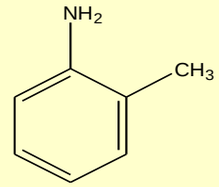
Harm reduction

- Which smoke toxicants are important?
- Over 5,000 chemicals identified in smoke
- Multiple reviews of toxicants in tobacco smoke
  - Hoffmann
  - Fowles & Dybing
  - TobReg
- Such lists influence regulators
  - Define chemicals for disclosure
  - Possible requirement for mandated lowering
- GR&D developing a framework to assess toxicants
  - External engagement with regulators
  - Internal assessment (product development)

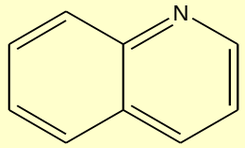
Polycyclic aromatic hydrocarbons



Aromatic Amines



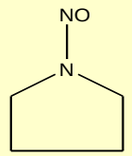
Aza-arenes



Aldehydes

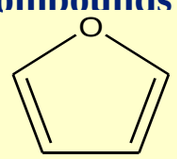
HCHO

N-Nitrosamines

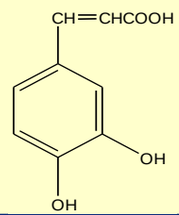


Inorganic Compounds (Metals)
Cd Ni Pb

Miscell. Organic Compounds



Phenols



World Health Organization TobReg proposal for mandated lowering of toxicants in smoke

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Table 1 Toxicants recommended for mandated lowering

Toxicant	Level in µg/mg nicotine (international brands)*	Level in µg/mg nicotine (Canadian brands)†	Criteria for selecting the value
NNK	0.072	0.047	Median value of the data set
NNN	0.114	0.027	Median value of the data set
Acetaldehyde	860	670	125% of the median value of the data set
Acrolein	83	97	125% of the median value of the data set
Benzene	48	50	125% of the median value of the data set
Benzo[a]pyrene	0.011	0.011	125% of the median value of the data set
1,3-Butadiene	67	53	125% of the median value of the data set
Carbon monoxide	18 400	15 400	125% of the median value of the data set
Formaldehyde	47	97	125% of the median value of the data set

*Based on data from Counts *et al.*[11]

†Based on the data reported to Health Canada minus the brands with NNN/mg nicotine levels over 0.1, which eliminates most US and Gauloise brands (http://www.hc-sc.gc.ca/hl-vs/tobac-tabac/legislation/reg/indust/constitu_e.html).[12]

NNK, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNN, *N*′-nitrosonornicotine.

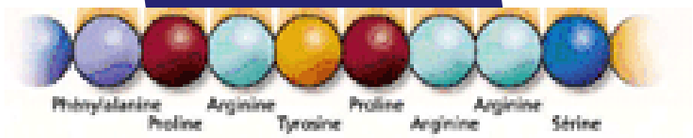
Additional compounds recommended for high priority for disclosure and monitoring:
acrylonitrile, 4-aminobiphenhyl, 2-aminonaphthalene, cadmium, catechol, crotonaldehyde, hydrogen cyanide, hydroquinone and nitrogen oxides

Burns *et al.* (2008) Tobacco Control

Selecting targets

Gene expression

Plant



Protein activity

Smoke chemistry

Product

Cured tobacco

Metabolite analysis

Important traits for sustainability

- Sustainability traits

  - Nitrogen use efficiency
  - Drought stress tolerance
  - Pest management
  - Herbicide management
  - Yield enhancement
  - Salt tolerance

The importance of the genome

- Multiple crops have sequenced genomes
  - Rice, Maize, Potato and Tomato.
- Great potential to support crop improvement

Genome sequence data

- Genes/promoters
- Genetic polymorphisms (Markers)

Transgenic

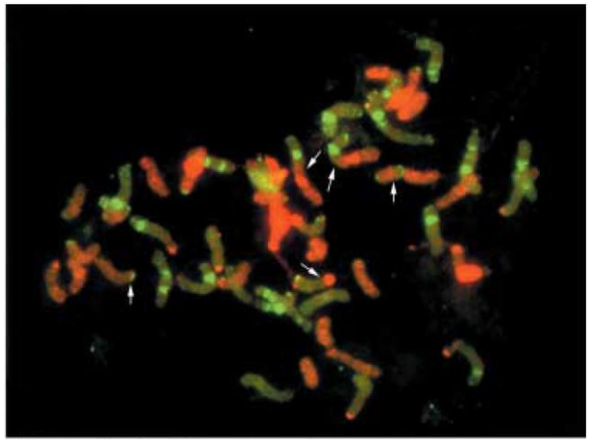
- Gene expression/silencing…

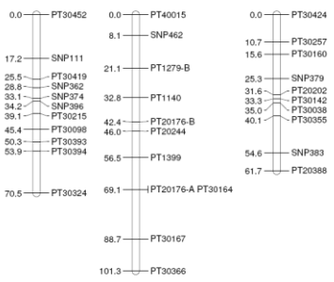
Molecular Breeding

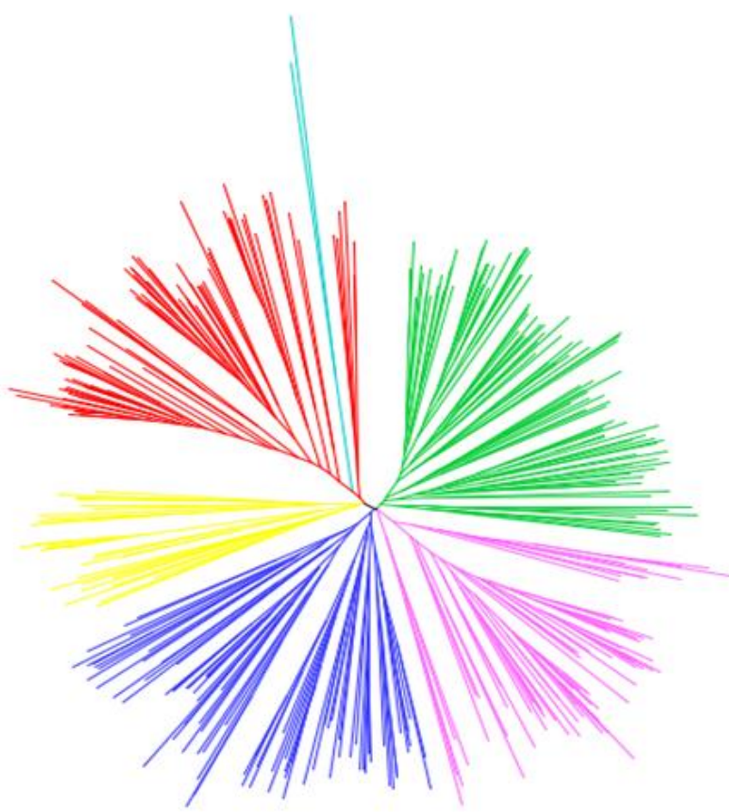
- QTL/GWAS
- Marker Assisted breeding

Our biotech platforms for tobacco and summary

- ATC developing tobacco sequence resources
  - Next Generation Sequencing technologies
- Identify the genetic differences between tobacco varieties- Molecular breeding
- Metabolite mapping precursor-toxicant
- Phenotyping HTP screening
- **New traits for harm reduction/sustainability**







Biotechnology for success