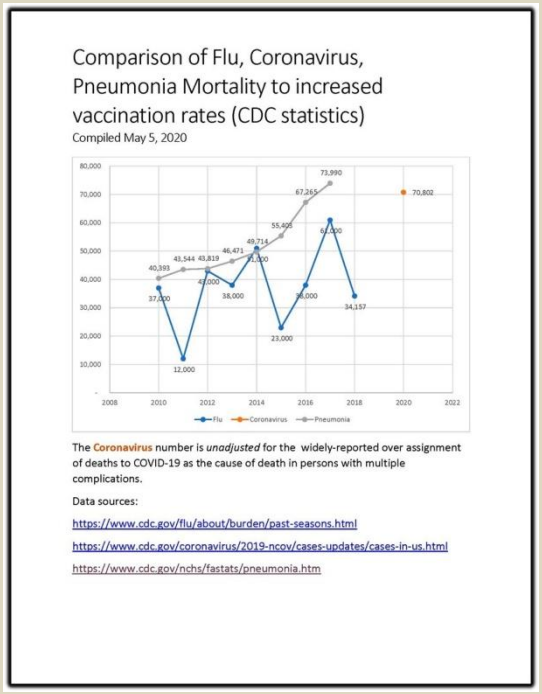
The British Rothschild Biowarfare Conspiracy

https://tinyurl.com/ybj29ueb

Pilgrims Society, Bill Gates, Tony Fauci, Pirbright Institute, NIH, CDC, Jacob Rothschild ("the cryptkeeper")* make $$$ billions from vaccines and vaccine research—are the very definition of ethical conflict of interest.

*** Rothschild Asset Management owns International Biotechnology Trust PLC, Co. No. 02892872 (UK) that controls massive U.S. biotech holdings**

Prosecute the American Pilgrims Society for sedition with the British Pilgrims Society in a conspiracy to attack the human blood stream



Open this chart as a PDF with hyperlinks

May 07, 2020—Conclusion from this CDC data review: The increases in mortality appear to have a direct accelerating correlation to the increased rates of vaccination.

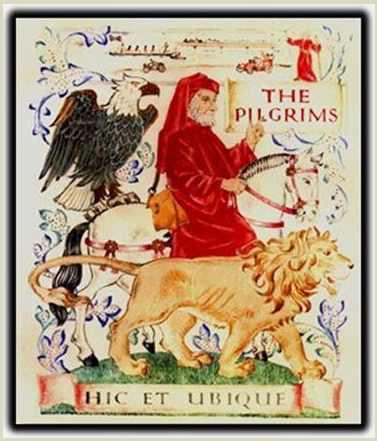
Since the prevailing assumption that vaccines should *reduce* flu mortality, the statistics appear to show that vaccines disproportionately *increase* flu mortality, not *decrease* it, as intended.

Let's stop injecting unknown foreign substances into our bloodstreams because some "expert" says its good, but where those experts have a political agenda as well as investments in the vaccine companies that will benefit.

Let's wake up and stop being so gullible. These so-called experts who fail to disclose their massive *conflicts of interest* is proof enough that they only have their self interest in mind, and not the welfare of *We the People* and our families.

Full analysis of CDC data.

Meet some of the Pilgrims Society (the literal "Deep State") eugenicists



L/R: **Jacob Rothschild**, 4th Baron Rothschild ("the cryptkeeper") owner of Rothschild Asset Management & Biotechnology Trust PLC, the first *DNA manipulation* biotech firm in the UK via father Baron Victor's company Biotechnology Investments Limited (BIL) (all records of this Rothschild-founded biotech firm are missing from Companies House UK and embargoed in archives until Jan. 2045); through BIL, Victor Rothschild (3rd Baron Rothschild) organized the modern version of The Pirbright Institute with Wellcome Trust and Bill Gates Foundation;

Anthony Fauci, NIH, creator of AIDS/HIV;

Deborah L. Birx, co-creator of AIDS/HIV with Fauci;

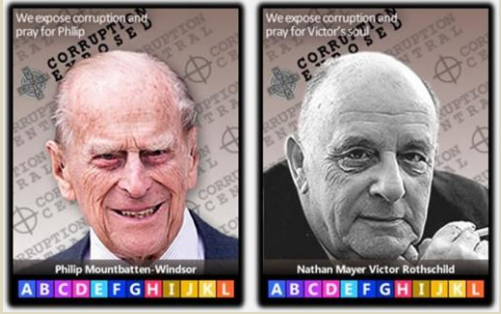
Bill Gates, global biotechnology vaccine glad-hander *par excellence*; and

Nick Knowles, virologist, director of the Foot & Mouth division of The Pirbright Institute, oversaw the 2007 foot and mouth outbreak at Pirbright UK, then oversaw the founding of **Merial Animal Health Institute** in *Nanching, China* for Pirbright, just four hours from *Wuhan, China*; Pirbright holds the U.S. Pat. No. 10,130,701 named "Coronavirus."

Prince Philip Mountbatten-Windsor

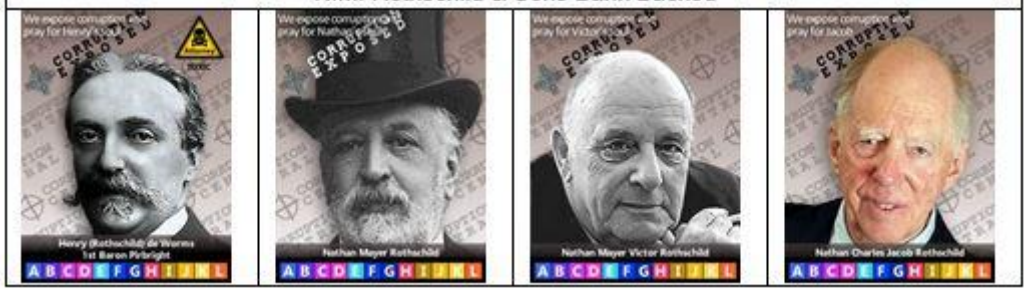
Longtime Patron of the Pilgrims Society

In a 1988 Freudian slip (given the now-known 120-year+ high priority of the Pilgrims Society for vaccines and eugenics), Philip famously told the German news agency Deutsche Press Agentur: "*In the event that I am reincarnated, I would like to return as a deadly virus, to contribute something to solving overpopulation*." Philip knew about the massive Baron Victor Rothschild investments (the Queen's banker) in the burgeoning DNA-manipulation biotechnology field that his company **Biotechnology Investments Limited (BIL)** was making (records are missing)—the first, initiated… in Britain. American venture capitalists beat a path to Rothschild's door after that. Ask why its company records are missing from Companies House and embargoed until 2045!



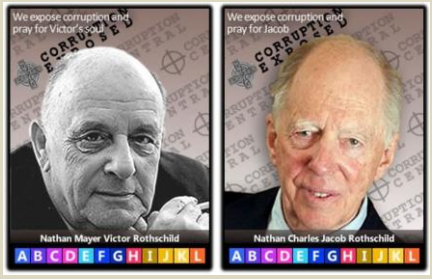
These are some of the people presently trying to *push* the world into mandatory vaccines, that at the very least, weaken, not strengthen, our immune systems. Let's dig a little deeper and see who is really hiding under the Queen's skirts, inside tech British Imperial Empire.

Henry de Worms (Rothschild)	Nathan	Victor	Jacob
1st Lord Pirbright	1st Baron Rothschild	3rd Baron Rothschild	4th Baron Rothschild
1840-1903	1840-1915	1910-1990	1936-
Collaborated and fund Henry Wellcome, Burroughs Wellcome & Co; funded Sir Henry Stanley to collect African pathogens; donated land for The Pirbright Institute; created the British South Africa Company; oversaw Rothschild funding of the BSAC and DeBeers; created Marconi Wireless monopoly; founder of the Pilgrims Society; sanctioned the killing of 60,000 Boers (French, German, Dutch) and Blacks (incl. 14,000 children) in the 2nd Boer War and the Wellcome vaccine experimentation in concentration camps	Funded Cecil Rhodes, British South Africa Company, DeBeers, helped set up the Rhodes Scholarship at Oxford, Privy Council, Rhodes executor, co-founded the Round Table, founder of the Pilgrims Society, co-organizer of the Imperial Press Conference, 1909; co-founder Empire Press Union, 1909, co-founder of MI5, MI6, GC&CS now GCHQ; sanctioned the killing of 60,000 Boers (French, German, Dutch) and Blacks (incl. 14,000 children) in the 2nd Boer War and the Wellcome vaccine experimentation in concentration camps	Bullied Parliament into unifying control of all R&D under the Pilgrims Society, incl. wireless, propaganda, pharma, intelligence; conspired with Nobel laureate Sydney Brenner to manipulate DNA and create novel "gain of function" killer viruses; sponsored Robert Lieber's missile, radar and satellite testing tied to biowarfare and David Sarnoff, RCA, NBC, Marconi, Navy, Army Air Force; member of the Pilgrims Society	Pushed Rothschild Asset Management control of daddy Victor's company Biotechnology Investments Limited (NIL), now International Biotechnology Trust PLC; member of the Pilgrims Society; funded Charles M. Lieber at Harvard to build and patent biowarfare nano technologies to take the Pilgrims Society eugenics attack to the **human bloodstream**
N.M. Rothschild & Sons Bank Backed			



Victor Rothschild is the British parliamentarian who almost single-handedly bullied Parliament to reorganize the British R&D under one UKRI umbrella (U.K. Research & Innovation) for optimal Pilgrims Society exploitation, including SERC(O), QinetiQ and The Pirbright Institute into the current time

Victor's son Jacob is carrying on that biowarfare activity



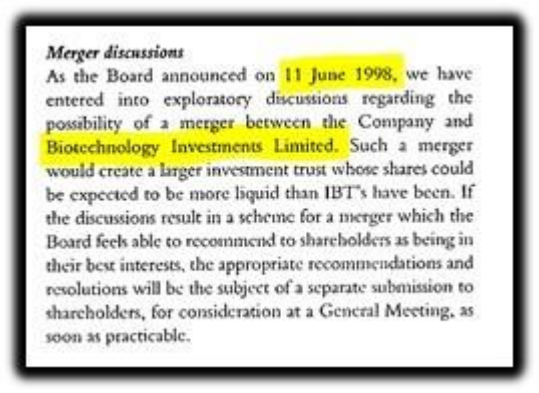
Victor's biotech mentor and partner in Biotechnology Investments Limited (BIL) was Nobel prize winner Sydney Brenner. BIL corporate documents and reports have been embargoed: "Closed until Jan 2045 – Suppress all images for 60 years".

http://libgallery.cshl.edu/items/show/70707

http://libgallery.cshl.edu/items/show/74744

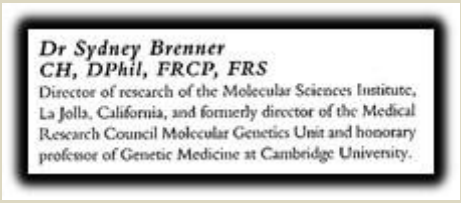
What are the Rothschilds hiding? Note also that BIL has been completely removed from Companies House. In 1999, it was merged into another Rothschild company: INTERNATIONAL BIOTECHNOLOGY TRUST PLC, Company number 02892872.

International Biotechnology Trust (IBT) PLC, Co. No. 02892872. (Filed Jan. 12, 1998). Annual Report and Accounts, 1998, incl. Biotechnology Investments Limited (BIL) merger, both Rothschild Asset Management companies. Companies House



Merger discussions

As the Board announced on 11 June 1998, we have entered into exploratory discussions regarding the possibility of a merger between the Company and Biotechnology Investments Limited. Such a merger would create a larger investment trust whose shares could be expected to be more liquid than IBT's have been. If the discussions result in a scheme for a merger which the Board feels able to recommend to shareholders as being in their best interests, the appropriate recommendations and resolutions will be the subject of a separate submission to shareholders, for consideration at a General Meeting, as soon as practicable.

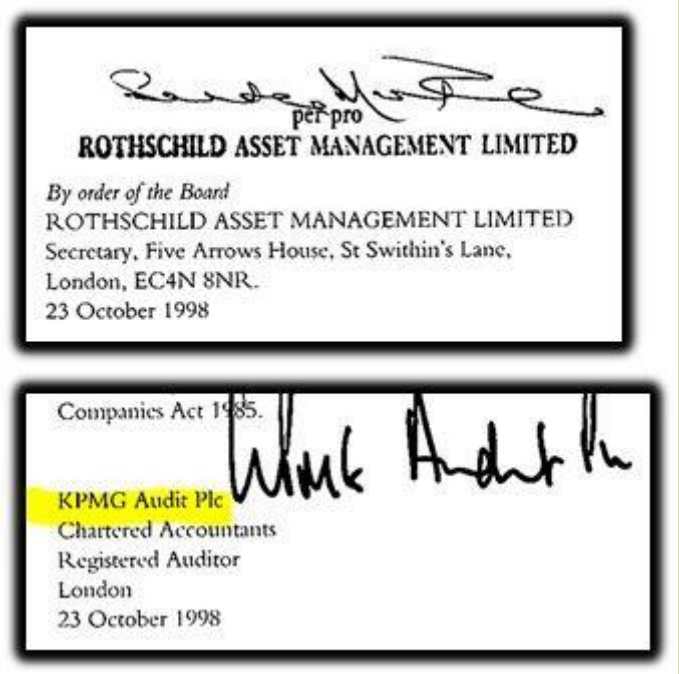


Dr Sydney Brenner
CH, DPhil, FRCP, FRS

Director of research of the Molecular Sciences Institute, La Jolla, California, and formerly director of the Medical Research Council Molecular Genetics Unit and honorary professor of Genetic Medicine at Cambridge University.

Substantial shareholdings
Ordinary shares

	Ordinary shares 25p
Co-operative Insurance Society Limited	12,261,467
Scottish Widows' Investment Management Limited	10,282,833
Sun Life Investment Management	9,359,896
Zeneca Limited	6,531,755
Lucas Pensions Trust Limited	5,828,329
Guardian Asset Management	5,646,442
Commerical Union Asset Management	3,882,044



per pro
ROTHSCHILD ASSET MANAGEMENT LIMITED

By order of the Board
ROTHSCHILD ASSET MANAGEMENT LIMITED
Secretary, Five Arrows House, St Swithin's Lane,
London, EC4N 8NR.
23 October 1998

Companies Act 1985.

KPMG Audit Plc
Chartered Accountants
Registered Auditor
London
23 October 1998

The Company owns more than 10% of the following companies, each of which otherwise stated:

Company	*Class of shares held*	*% of class held*
Anergen Inc	Common	12.9
Core Group (incorporated in UK)	Ordinary	12.7
Targeted Genetics	Common	11.9
Ribozyme Pharmaceuticals Inc	Common	11.1
Cubist Pharmaceuticals Inc	Common	10.6
Netgenics	Series D Preferred	10.6
Cytel	Common	10.0

at 31 August 1998

	Value £000	*Book cost* £000	Investee company statistics as at date of last audited results: *Proportion of investee company's capital owned*	*Notes*	*Proportion of investee company's assets attributable to investment*, £000	*(Loss) per share* £
Core investments						
SUGEN	4,949	4,849	4.6	1	1,371	(1.50)
Vanguard Medica**	3,007	5,514	4.3	1	2,318	(0.85)
Netgenics*	2,986	3,000	10.6	1	203	***
MorphoSys*	2,921	2,809	9.7	1	681	***
Onyx Pharmaceuticals	2,682	4,959	9.9	1	1,735	(1.00)
Angiotech Pharmaceuticals	2,539	2,992	6.0	2	288	***
Core Group	2,397	5,336	12.7	1	2,983	(0.17)
Targeted Genetics**	2,253	5,257	11.9	1	404	(0.43)
Corvas International**	2,090	4,628	9.3	1	1,269	(0.11)
Cytel	1,956	4,833	10.0	1	1,483	(0.34)
Anergen	1,912	3,136	12.9	1	611	(0.27)
Medarex	1,829	3,168	3.9	1	135	(1.78)
Cubist Pharmaceuticals	1,583	4,068	10.6	1	1,228	(0.15)
Biocompatibles International**	1,539	6,903	2.2	1	444	(0.39)
Cadus Pharmaceuticals	1,523	3,815	6.5	1	1,600	(0.27)
Geltex Pharmaceuticals	1,523	2,426	0.9	1	292	(1.09)
Cell Therapeutics	1,470	9,472	8.8	1	3,839	(1.10)
Ribozyme Pharmaceuticals	1,436	5,805	11.1	1	1,273	(1.24)
LocalMed*	1,344	1,952	4.2	1	85	(0.78)
Non-core investments						
Microcide Pharmaceuticals	299	909	1.1	1	325	(0.26)

Classification of investments by value

at 31 August 1998

	Total 31 August 1998 %
Equities - North America	
Pharmaceuticals:	
Quoted	66
Unquoted	10
Equities - UK	
Healthcare	
Quoted	4
Pharmaceuticals	
Quoted	13
Equities - Europe	
Pharmaceuticals:	
Unquoted	7
Total	100
Number of individual holdings:	*No.*
Target investments	19
Shorter term investments	1
Total	20

Biotechnology Investments Limited (BIL) (established, 1981) was Europe's first specialist biotech investment company, funding early-stage and unlisted biotechnology companies. Dr. Brenner was one of six eminent scientists hired as an advisor to BIL (under the direction of Rothschild Asset Management) for the purpose of gathering the most accurate technical and financial information about these start-up companies. Dr. Brenner reviewed their research, project reports, staffing and business plans and reported his findings back to BIL. The documents in this

subseries are the notes he created about the companies and their potential as investment entities, as well as some correspondence regarding those companies. Further documents could be found throughout the Rothschild Assent Management folders. http://libgallery.cshl.edu/items/show/82757

http://libgallery.cshl.edu/items/browse/tag/Brenner,%20Sydney

Sydney Brenner CH FRS FMedSci MAE (13 January 1927 – 5 April 2019)

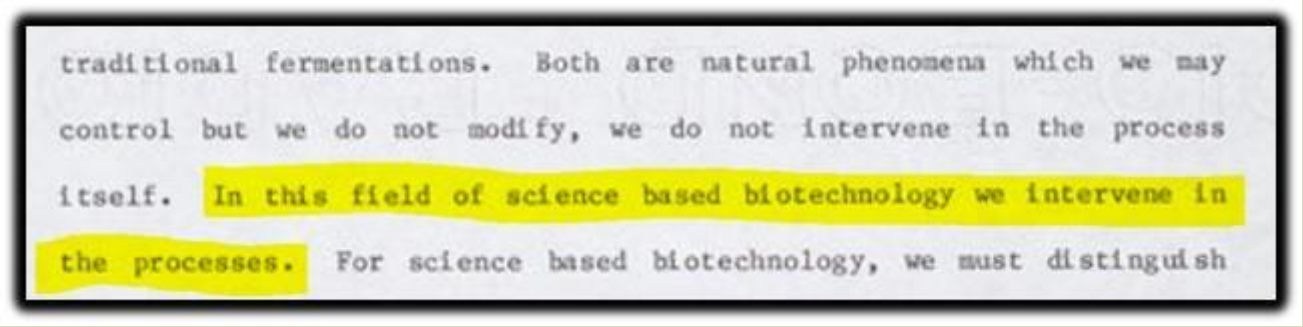
https://en.wikipedia.org/wiki/Sydney_Brenner

…was a South African biologist. In 2002, he shared the Nobel Prize in Physiology or Medicine with H. Robert Horvitz and Sir John E. Sulston.[1] Brenner made significant contributions to work on the genetic code, and other areas of molecular biology while working in the Medical Research Council (MRC) Laboratory of Molecular Biology in Cambridge, England. He established the roundworm *Caenorhabditis elegans* as a model organism for the investigation of developmental biology,[2][16] and founded the Molecular Sciences Institute in Berkeley, California, United States.[17][18][19][20][21][22][23][24]

Here's what Brenner was thinking as he helped spawn the modern biotechnology investing world in all its juvenility and irresponsibility, that may kill us all.

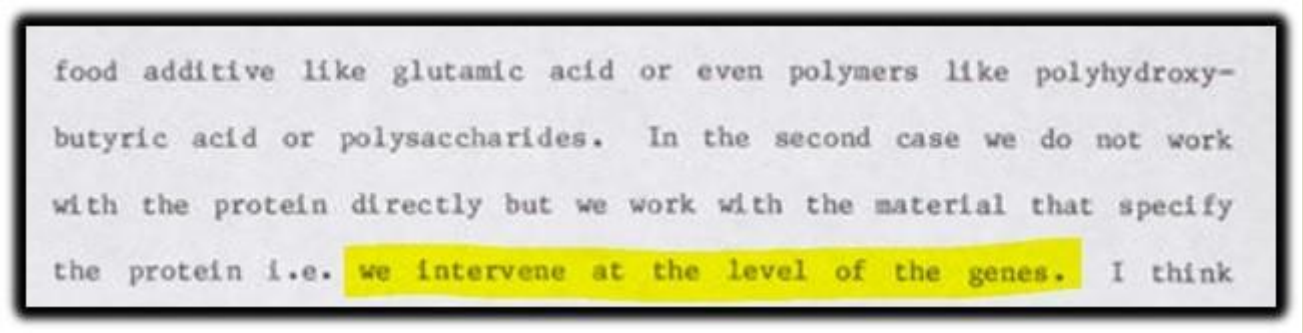
Sydney Brenner. (Nov. 14-18, 1983). Overview of Biotechnology in Industry – Keynote Address, Seminar on Biotechnology – Singapore, Ref. SB/3/23, No. 74175. CSHL Archive Repository.

https://www.fbcoverup.com/docs/library/1983-11-14-Sydney-Brenner-Overview-of-Biotechnology-in-Industry-Keynote-Address-Seminar-on-Biotechnology-Singapore-Ref-SB-3-23-No-74175-CSHL-Archive-Repository-Nov-14-18-1983.pdf



traditional fermentations. Both are natural phenomena which we may control but we do not modify, we do not intervene in the process itself. In this field of science based biotechnology we intervene in the processes. For science based biotechnology, we must distinguish

http://libgallery.cshl.edu/items/show/74175



food additive like glutamic acid or even polymers like polyhydroxy-butyric acid or polysaccharides. In the second case we do not work with the protein directly but we work with the material that specify the protein i.e. we intervene at the level of the genes. I think

factory that is manufacturing TV sets. There are 2 ways in making modification to the TV sets - one is to get to the factory floor and alter each TV set, that will be operting at the level of the protein which we are now at, the other one is to get into the office of the factory where the blue prints are kept which tell people how to make TV sets and alter the instructions there and from that part on that factory will produce the modified TV sets I think that it is very important to distinguish between operating on the working machinery, of the cells and working on the specification of the working machine. It is not merely a quantitative difference but an absolute qualitative difference and requires a completely new approach to the subject. Let me now try to give you a very general picture of how

biotechnology and is the field where we intervene directly in the process and try to remould it rather than merely use it as in the traditional applications of fermentation. For science based biotechnology I would like to think that there are two distinct phases; a more classical one based on natural products chemistry and biochemistry, particularly enzymology, and the modern phase which is based on genetics and molecular biology.

has been at the level of the ~~[illegible]~~ ~~[illegible]~~ phenotype. ~~[illegible]~~ I
happen to be great believer in these ~~often~~ genetic engineering

6

methods; ~~[illegible]~~ but
the gene cloning methods also allow us to cross genetic
barriers far more readily than they are abrogated in Nature

They allow us to extend horizontal transmission of
genetic information which in Nature is largely vertically
transmitted.

product is used for. Much of medical advances in biotechnology is to make products available in abundance for which people are looking for diseases rather than having diseases for which people are looking at products.

Discuss added genetic elements, episomes and viruses
Brief discussion of cloning in bacteria addition of functions.

Health Care

← Prev

Date
1983

Identifier
SB/4/1/189

Location
Collection SB: Sydney Brenner Collection (1927-2010)
Series SB/4: Subject Files (1949-2009)
Subseries SB/4/1: Subject Files - General (1949-2009)

Author/Creator
Brenner, Sydney
Rothschild, Nathaniel Mayer Victor
Rothschild, Baron, 1910-

Subjects
Biotechnology
Advisory Committees
Science and Engineering Research Council (Great Britain)

Description
(Include handwritten reports by Brenner and correspondence with Lord Rothschild regarding biotech investments)

http://libgallery.cshl.edu/items/show/74414

LORD ROTHSCHILD

Telephone: 01-280 5000
Telex: 888031

N.M. Rothschild & Sons Ltd.
New Court
St. Swithin's Lane
London EC4P 4DU

20th December 1983

Dear Sydney,

Is there anything in these two pieces of paper of a shortish-term nature, i.e. something or somethings which we might be interested to support ?

Please check with David L.

These papers were presented at a meeting organised by the new company formed to exploit ARC findings. I know that David Leathes and Peter Laing attended this meeting and I believe that we could support this only by investment in the new company. We were not allowed in at the beginning but I think we should have an opportunity at a later stage. The venture group that was allowed in with the BTG was Advent; I did persuade them to see Leathes but we got no further. S.

Of the 63 ventures given by CW Ventures:

(a) (12) are in the existing BIL area; about ½ of these involve immunoassay.

(b) The following could go into a slightly extended BIL: (25)

1. Diagnostics 5
2. Biomedical Instrumentation 6.
3. Electromagnetic fields, sonic, nuclear medicine 3.
4. Devices + prostheses 4
5. Patient monitoring 2
6. Special medical materials, blood purification 5

(c) A special group which could quite easily go into an extended BIL but which I think we would have to make judgments after we talk to Channing Wenberg

1. Pharmaceuticals of classic kind (9) The question is whether any of these ventures can succeed in competition with the resources of the major pharmaceutical companies and should they be excluded unless they have some special molecular technology
2. Computer systems (software). Of the list given I would judge only one to be appropriate to an extended BIL and that is on diagnosis software. (1)

(d) A number of projects which may be difficult to add or extended except by making a major change

1. Computer systems for financial management,

~~600~~ pharmacy automation and 2 educational systems, a ~~total~~ of (5) projects

2. Distribution services, hospital services, centres and clinics, management services (11)

Thus only 16 of the 63 projects, about 1/4, would be excluded from an extended BIL.

· One may look at the 10 ~~approved~~ investments made by CW Ventures.

- 2 are in BIL's existing field; in fact we are an investor in one of them.
- 6 would fit into the somewhat extended area, being in diagnostic imaging, instrumentation, devices & products.
- 2 would be in the excluded category
  - medical records software
  - outpatient obesity clinics.

These notes are ~~not~~ meant only to state ~~a~~ propositions

Sydney

With Compliments

I enclose a copy of the notes that Channing, Weinberg used in their presentation to us on Monday. I also enclose the summary business Plan for Inomedix, whom we met in New York. These people developed a disposable thermometer for a subsidiary of Akzo. (I have enclosed one for you to try - its a neat idea) (use under tongue as normal!) We think that this proposal is quite promising. They are looking for $1m for 40% of the equity.

N M Rothschild
Asset Management Limited

PO Box No 185
New Court
St Swithin's Lane
London EC4P 4DU

David

Health Care Investment

I have made an analysis of the 63 ventures by CW as a sample of recent projects they evaluated. They can be divided as follows

(a) 12 (numbers 2, 8, 9, 11, 13, 25, 30, 31, 33, 4
63) are in biotechnology and very similar
projects we consider.

(b) if we were to extend the field of BIL to incl
based medical technology use this would en cau
following projects

(i) Diagnostics 5 (numbers 3, 10, 49, 57, 59)
(ii) Biomedical Instrumentation 6 (numbers 6, 1
(iii) Electromagnetic fields and nuclear medicine 3
12, 35, 42)
(iv) Devices and prostheses 4 (21, 29, 60, 61)
(v) Patient monitoring 2 (22, 36)
(vi) special materials, blood purification etc 5 (n
54, 58 and

This is a further 25 projects.

(c) In addition the extended area could ac
the following:

(i) Pharmaceuticals 9 (numbers 7, 14,
48, 51 and 56)

The only question here is whether this is a fie
should enter at all because of the predomin
established pharmaceutical companies in this
should ask Charming Wenberg at their se

totally exclude; ~~Office only~~ Thus only 16 of the 63 projects, about a quater would be eliminated from an extended BIL.

One may also look at the 10 investments made by CW Ventures

- 2 are in BIL's existing field (in fact we are invested in Queue Systems)
- 6 would fit into the extended area
- 2, the medical records software and the outpatients obesity clinic would be excluded.

~~The~~ Thus is not significantly different from the analysis of the larger group of projects.

Sydney Brenner
Jan 8 1984

CW Ventures report ~~to~~ and letter to Bob Pirie

- Average investment $ ½M

1. Gambro AB - dialysis - expand membrane technology
   immunotherapy
   electronic devices.
   therapeutic blood filtration
   large company $ 1,618,000

2. Quinton Systems BIL already has investment
   CW : $ 606,787

3. Gabrieli M I Systems - Medical records software
   - proprietary technology
   (start up)

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1. Quantum Medical Systems — Ultrasonic diagnostic imaging
2. Diamond Electro-Tech — Gas + Blood electrolyte analyzer
3. Microsonics — Image analysis systems.
4. General Immunoassay Inc — interested in infection.
5. Monmouth Laboratory Inc. — laser systems.
6. Stervet Laboratories — Equine products (hyaluronan and)
7. Nutritional Management — (Out patient obesity clinics).

We have found it somewhat surprising that many of the investment opportunities we see are already established ventures..... we are seeing more such situations than we had originally anticipated. As a result it is difficult to justify making investments in the many research & development type projects that come to us, which, because of their pre-venture stage, offer substantially higher risks. But we're looking and looking at possibility of "seed" or "feeder" funds to work in this pre-venture situation.

* May be in existing area

Biotechnology

63 Radio immunoassay

62 - synthetic bone graft material

61 - artificial kidney device:

In existing area of BIL

- 2 hybridoma, peptide synthesis (Fredrik)
- 8 Diagnostics R&D
- 9 Immunological products for diagnosis
- 11 Cell Culture
- 13 Plant molecular genetics (Ringve)
- 25 biochemical raw products suppl.
- 30 Monoclonal antibodies
- 31 Vaccines tech ? Immunobiological products
- 41 Microb biol screening for new pharmaceuticals and commercial
- 55 Genetic engineering
- 63 Radio immuno assay products

In extended area.		Exclude from extended area
3	39	1
6	40 ? →	4
7 * Pharmaceuticals	42	5
10 *	43 ?	17
12	44 pharmaceuticals.	18
14	46 →	~~19~~
15 pharmaceuticals	48 pharmaceuticals	23 ?
16	49 Clinical diag	24
20 -	50 (?)	27
21	51 (?) pharmaceuticals	28
22	53	~~33~~ 32
26	54	37
29	56 pharmaceuticals.	45 Medical information system ?
~~33~~	57	47 Educate computer.
34 ? ~~?~~	58	52 dispensing system
35	59	
36	60 (?)	
38 pharmaceuticals	61	
	62	

Of the 63 projects listed in Oklahoma City CW ventures

12 are already in BIL's area
and of these 6 would be in are in immunology
focusing on immunoassay.

Of the remainder would put the following into
the extended area:
They fall into the following fields.

Diagnostics 3, 10, 49, 57, 59

Biomedical Instrumentation 6, 16, 20, 26, 39, 53,

Pharmaceuticals 7, 14, 15, 38, 43, 44, 48, 51, 56,

~~Medical processing~~

Electro magnetic fields } 12, 35, 42,
nuclear medicine }

Devices & prostheses 21, 29, 60, 61,

Monitoring – 22, 36
Synthetic bone material – 62,
Water purification – 50,
Blood handling – 54,
poly urethane plastics 58, Dentine material 19

Computers / Communications

32 : computer system with financial capabilities OUT
34 : hospital pharmacy automation
40 : Medical computer consultants OUT
45 : Medical information system
46 : Software for diagnosis & management IN
47 : computer communication syste for improved worker effectiveness.

Excluded:

Distribution services 1

Service, Centres 4, 5, 17, 18, 24, 27, 28, 37

Technology Transfer ? 23
Dispensing system 52
~~Medical computer system~~
~~Computer~~

Lord R
David Leathers.

The Health Sciences Project

We will need a distinctive approach, and defining it is important because it will differentiate us from others already in the same field and will also limit the area of health care which we should emphasize in the initial phase, at least.

I believe we should base our entry on the special position we have achieved in BIL but we need to take care that we do not dilute this achievement. The new activity should complement BIL which already has several investments in companies whose main thrust is in the health care area. Thus the new fund could look particularly for opportunities which exploit the products of the biotechnology companies and carry them into different and new market sectors, as specialized health care companies. Many of the applications require the fusion of several technologies which may require a new group of people with different skills. Also by looking at the final target areas we may find gaps in the R and D level which we may want to fill.

To fix ideas, I enclose a classification of the R+D and applications areas for a number of health care activities. It shows that there are gaps at the R+D level particularly in specialized instrumentation and it also shows that there are opportunities in the diagnostic field for applications appropriate to a doctors office or the patients home. I need to expand many of the entries; are there any blatant omissions?

Sydney Brenner
Nov 30 1983

IN VITRO DIAGNOSIS		APPLICATION SECTORS ①			
RELEVANT INVESTMENT	RESEARCH & DEVELOPMENT	PUBLIC HEALTH GOVERNMENTAL	INSTITUTIONAL HOSPITALS, LABORATORIES	PROFESSIONAL DOCTORS OFFICE	PERSONAL HOME
Genetic Systems Centocor Cell Tech	Monoclonal Antibodies.	Tropical diseases, Epidemiology Toxicology	Clinical diagnosis Drug monitoring	Clinical diagnosis Drug monitoring	Home diagnosis e.g. pregnancy, drug monitoring
Amgen Integrated Genetics Chiron	Antigens by rec DNA (and synthesis)	as above	as above	as above	—
Genzyme	Enzymes by Screening & rec DNA	– Toxicology	clinical diagnosis drug monitoring	clinical diagnosis drug monitoring	drug monitoring
Integrated Genetics	DNA probes by rec DNA	Genetic screening Toxicology	Diagnosis of genetic disease; Virus & bacterial diagnosis.	—	—
IQ Bio Applied Biosystems	Instrumentation Chemical, Physical, Computer	Special assays for field conditions	Biosensors, Novel assays, Automation of clinical chemistry and microbiology especially antibiotic sensitivity assays.	Adaptation of assays to doctors office. Biosensors	Special assays required, may include biosensors.

IN VIVO DIAGNOSIS		APPLICATION SECTORS ②			
RELEVANT INVESTMENT	RESEARCH & DEVELOPMENT	PUBLIC HEALTH GOVERNMENTAL	INSTITUTIONAL HOSPITALS, LABORATORIES	PROFESSIONAL DOCTORS OFFICE	PERSONAL HOME
Genetic Systems Centocor Cell Tech	Monoclonal Antibodies	—	Imaging; Implants. biosensor	Implant biosensor	Implant biosensor
	Enzymes by Screening + rec DNA	—	Implant biosensor	Implant biosensor	Implant biosensor
	Instrumentation				
	Chemical	—	Modification of antibodies and enzymes for sensors, and imaging; Use of labels.		non-radioactive
	Physical - ultrasound - NMR - Scanners	—	non invasive imaging sensor development		
	Computer	—	Analysis of results		

THERAPY & PROPHYLAXIS		APPLICATION SECTORS ③			
RELEVANT INVESTMENT	RESEARCH & DEVELOPMENT	PUBLIC HEALTH GOVERNMENTAL	INSTITUTIONAL HOSPITALS, LABORATORIES	PROFESSIONAL DOCTORS OFFICE	PERSONAL HOME
Genentech Amgen Repligen Chiron Immunex Cell Tech	Recombinant DNA products - new therapeutic agents, vaccines.	vaccination programmes.	Once proven, like other pharmaceuticals	like other pharmaceuticals	
Genetic Systems Centocor	Monoclonal Antibodies		Targetted therapy Cell fractionation	targetted therapy	
	Gene replacement therapy		Repair of somatic cells.		
	Instrumentation Chemical Physical Computer		Drug delivery systems with automatic regulation using biosensors as developed for in vivo diagnosis.		
	Organic Chemistry Drug development Classical area of pharmaceutical companies.				

To: Lord Rothschild 28th November, 1983

From: Peter Laing

Subject: Health Care

I doubt that a precise definition of "Health Care" exists as the term is deliberately vague so as to encompass every actual and potential activity related to the field. However, I would suggest this as my best effort:-

"The supply of products and services associated, either directly or indirectly, with the prevention, detection and treatment of disease, disability or injury."

This is broader than, say, "Medical Technology" in that it includes such important (if unspectacular) areas as Provision of Hospital Management and Housekeeping Services, Drug Wholesaling and Dispensing, Computer Software for the Operation of GP Practices and Manufacture of Hospital Beds.

I attach a list of major Health Care areas. I apologise for the fact that I have not had enough time to make the list either comprehensive or ranked in order of importance.

HEALTH CARE SECTORS

PREVENTIVE MEDICINE (includes VACCINES AND GENETIC SCREENING)

DIAGNOSTIC TESTS - Clinical Laboratory/GP's Surgery/Home

DIAGNOSTIC INSTRUMENTATION - Gamma-Counters/Fluorimeters/
Enzyme Reactors

CLINICAL LABORATORIES

DIAGNOSTIC IMAGING - X-ray, Nuclear Medicine, CAT scanners,
Digital Angiography, Nuclear Magnetic
Resonance, Ultrasonics, Thermography

ETHICAL PHARMACEUTICALS - Prophylactic and therapeutic agents
distributed among 18 major therapeutic
classifications and 90 sub-classes

PROPRIETARY MEDICINES

DRUG DELIVERY SYSTEMS

DRESSINGS AND APPLIANCES - (includes WOUND CLOSURE DEVICES)

ETHICAL WHOLESALING - Hospitals/Pharmacies

HOSPITAL OPERATION AND MANAGEMENT -
Surgical/General/Psychiatric/
Alcohol or Drug Abuse/Local/Outpatient/
Homecare

HOSPITAL HOUSEKEEPING AND MAINTENANCE SERVICES

MEDICAL COMPUTERS AND SOFTWARE - Diagnosis/Hospital
Management/G P Management

SURGICAL INSTRUMENTS (includes LASERS)

ANAESTHESIA AND LUNG-FUNCTION EQUIPMENT

OPERATION AND RECOVERY ROOM EQUIPMENT

PATIENT MONITORING

BLOOD PROCESSING EQUIPMENT

PLASMAPHERESIS

INFUSION PUMPS AND SOLUTIONS

DIALYSIS EQUIPMENT

PAIN CONTROL

SURGICAL IMPLANTS AND PROSTHESES

CARDIAC CARE EQUIPMENT (includes PACEMAKERS)

OPTHALMIC EQUIPMENT - Testing/Surgery

NUTRITION - Hospital/Home (includes OBESITY CONTROL)

TOXICOLOGY TESTING

OBSTETRIC AND NEONATAL EQUIPMENT

BIOSENSORS

CANCER DETECTION AND THERAPY

ALLERGIES

ORTHOPAEDICS

DENTAL PRODUCTS

DERMATOLOGY

20-XI-95

A SELECTION OF EMERGENT MEDICAL TECHNOLOGIES

1. Nuclear Magnetic Resonance for three-dimensional imaging of soft tissue organs.

2. Implantable insulin pumps with feedback control using a glucose biosensor.

3. Ultrasonic monitoring of cardiac output using Doppler shift.

4. Therapeutic apheresis for control of autoimmune diseases.

5. Biocompatible artificial skin for burn patients.

6. Cancer therapy using laser irradiation of tumours dosed with haematoporphyrin.

7. DNA hybridisation probes for screening for genetically-inherited diseases such as cystic fibrosis.

8. Transdermal delivery of drugs which do not survive oral administration.

9. Treatment of impotence using an erectable penile prosthesis.

10. Targetting of drugs or radioisotopes using monoclonal antibodies directed against the desired site of action.

Peter Laing
30th November, 1983

Sydney - this seems just what we want. It will probably end up taking a whole day. David.

CHANNING

CHANNING, WEINBERG & CO., INC. / 950 THIRD AVENUE / NEW YORK, NEW YORK 10022 / (212) 753-8922

WEINBERG

December 8, 1983

Mr. David Leathers
N.M. Rothschild & Sons, Ltd.
New Court, St. Swithens Lane
London EC4P - 4DU
England

Dear David:

It was good to hear from you and we look forward to having you and Dr. Sidney Brenner join us in New York.

The outline I envision for our session follows. Depending on your availability and desire, the mini-seminar should last 4-6 hours. I will corral several of our consultants in order that you will benefit from several perspectives in addition to breaking the monotony of one speaker for such a long period.

Section I

- o Overview of the changing U.S. medical supply, equipment, device and service market.
    - o What's included
    - o Size and growth rate
    - o Factors affecting the field
        - demographics
        - evolving technology
        - cost containment
        - changing medical practice

Section II

- o Promising markets and companies/areas to avoid
    - o Review of the Channing, Weinberg Price-Performance Model
    - o How major health care companies are coping with change
    - o Dull Products/Markets
    - o Promising Products/Markets
    - o Promising Service Areas

I hope this fills the bill. As discussed, there is no fee for this session. We would all enjoy getting to know you and Dr. Brenner better.

Sincerely,

L. John Wilkerson

L. John Wilkerson
Executive Vice President

signed in absence

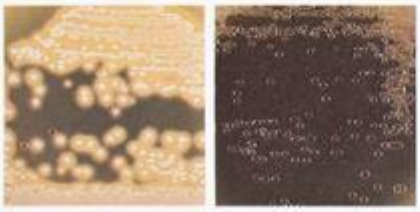
Genetic Manipulation of Crop Plants

DEVELOPMENT OF STARCH DEGRADING YEASTS USING GENETICALLY ENGINEERED PLANT GENES

The fermentation of starch to ethanol is an important industrial process. When the source of starch is a cereal seed, as used in the brewing industry, the starch is broken down to sugars and oligosaccharides by enzymes synthesised by the germinating seeds. The sugars are then converted to ethanol by yeast. The conversion of carbohydrate to ethanol necessarily involves the combined action of plant enzymes and yeast because the commonly used industrial yeasts do not produce the enzymes necessary to degrade starch. Although germinating cereal grains are an excellent source of enzymes for breaking down starch, in recent years similar enzymes produced in other microorganisms have been added to the fermentation tanks to carry starch degradation to completion more efficiently.

New yeast strains

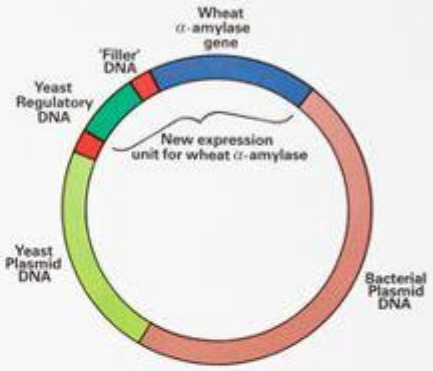
An alternative approach is to create yeast strains that are capable of using starch substrates directly because they can produce their own complement of starch hydrolysing enzymes. One way of creating such yeast strains is to use genetic engineering techniques to insert the appropriate genes for the starch degrading enzymes into yeast from other organisms. This approach has been initiated by the Plant Breeding Institute where a major gene for starch degradation, specifying α-amylase, has been isolated from wheat and transferred into yeast. Wheat α-amylase is synthesised in large quantities when wheat seeds germinate and its role is to break down the starch in the seed. The protein contains a special peptide which ensures that it is exported out of the plant cells to attack starch elsewhere.



Yeast plated on medium containing starch and exposed to iodine vapour. (Left) yeast containing the α-amylase gene. (Right) control yeast.

Wheat genes into yeast

The genetic engineering of the wheat genes into yeast was carried out as follows: A wheat gene for α-amylase was synthesised in the test tube by making a DNA copy of messenger RNA molecules isolated from germinating wheat grains. The DNA copy was inserted into a plasmid and introduced into the bacterium *Escherichia coli*. Large quantities of the α-amylase gene were purified from a culture of the modified bacteria. To ensure the expression of the α-amylase gene in yeast it was necessary to join regulatory DNA signals from yeast to the plant gene. A piece of DNA from a yeast gene was therefore joined to the α-amylase gene to provide signals to ensure that yeast would synthesise a messenger RNA molecule containing the plant gene and also would translate the α-amylase protein from the messenger RNA. This newly constructed DNA was then inserted into a plasmid that can replicate in yeast cells.



Vector constructed for insertion into yeast to achieve replication and expression of wheat α-amylase gene.

Modified yeast

The modified yeast cells containing this plasmid made the enzyme α-amylase, as predicted from the structure of the newly inserted DNA. Of even greater interest was the finding that the yeast cells recognised the special peptide on the wheat α-amylase and exported the enzyme out of the yeast cell. Consequently when the engineered yeast cells were cultured on medium containing starch, the yeast cells degraded the starch, leaving colourless halos around the colonies after exposing the plate to iodine which stains starch purple.

The yeast cells with the wheat α-amylase gene cannot degrade all the starch to simple sugars since they need some of the other enzymes found in germinating cereal grains. Further development of an efficient starch degrading yeast will require the transfer and expression of a full complement of starch degrading enzymes from plants or other organisms. Furthermore, the genes will need to be transferred to industrial strains of yeast. However, the work reported here represents an important beginning for the commercial production of starch degrading yeasts. It is also a good example of the new possibilities that are emerging from the development of genetic engineering techniques. The properties of microorganisms and plants can now be changed in very specific ways to adapt them to industrial needs.

Dr S. Rothstein, Dr A. A. Gaterby,
Dr D. Baulcombe & Dr C.M. Lazarus
Plant Breeding Institute
Trumpington
Cambridge
Telephone: (0223) 840932

Agricultural and Food Research Council, 160 Great Portland Street, London W1N 6DT. Telephone: 01-580 6655

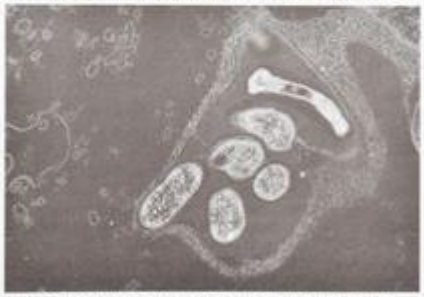
Genetic Manipulation of Crop Plants

CLONING THE NODULATION GENES OF RHIZOBIUM

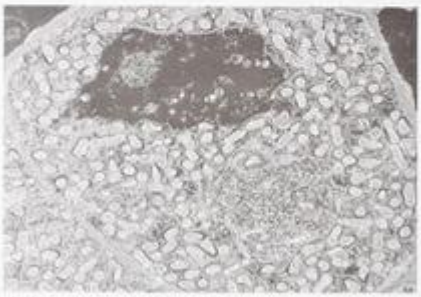
The roots of legumes such as peas, clover and beans possess nitrogen-fixing nodules which are induced by different species of *Rhizobium* bacteria. Thus these plants can grow well in the absence of nitrogenous fertilizer as long as they are infected with the correct strain of *Rhizobium*.

Root hairs from peas are deformed following inoculation by a nodulating strain of *R. leguminosarum* (left) but not by a non-nodulating mutant (right).

The infection process and the subsequent development of nitrogen-fixing nodules occurs via a series of well defined morphological stages. Initially the rhizobia attach to the plant root hair and induce a characteristic curling of the root hair and the bacteria then enter the root hair. In a successful infection the root hair cell nucleus migrates towards the point of bacterial entry, and then appears to return, followed by an infection thread containing the growing bacteria. This infection thread grows and branches within the root, and there is an activation of meristematic growth which results in the development of a root nodule. The bacteria are then released from the infection thread and are surrounded by a peribacteroid membrane. The bacteria then increase in size and develop into the pleiomorphic bacteroid-form which is active in

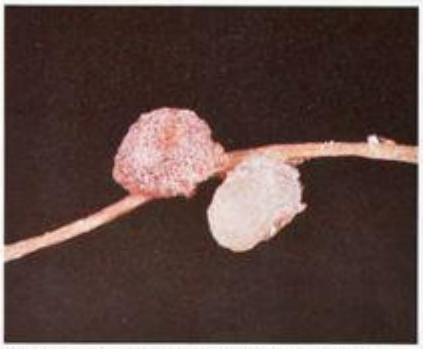


Electronmicrograph of infection thread containing *Rhizobium* cells.



Bacteroids within a plant nodule cell.

nitrogen fixation. As the nodules reach maturity they become pink due to the production of a protein called leghaemoglobin. This molecule has a similar structure to mammalian haemoglobin and carries oxygen to the bacteroids which require large amounts of oxygen during nitrogen fixation.



Two pea nodules: the pink one is infected with a normal strain and the pale one contains a non-fixing mutant.

Specificity of symbiosis

One feature of the symbiosis is that it is specific. For example the species *Rhizobium leguminosarum* nodulates peas and not *Phaseolus* beans whereas *R. phaseoli* nodulates beans but not peas. Despite its importance, we do not know, at a biochemical level, what is so special about leguminous plants which allows them to be nodulated, nor, conversely, do we understand what gives *Rhizobium* the special ability to infect these plants.

The approach to this problem at the John Innes Institute has been to identify and characterise the symbiotic genes of *R. leguminosarum*. These have been shown to be on plasmids, some of which can be transferred to other species of *Rhizobium*, thereby allowing them to nodulate peas rather than, for example, clover.

Analysis of genes

To analyse these plasmid-borne nitrogen fixation, nodulation and host range genes, they have been cloned and mapped by recombinant DNA techniques. The nodulation genes lie between two clusters of nitrogen fixation genes and the whole 'symbiotic' region spans approximately 50,000 base pairs of DNA. Given the complexity of the infection process surprisingly few bacterial genes appear to be required for nodulation and the determination of host range. By transferring the cloned nodulation genes of *R. leguminosarum* into *R. phaseoli*, nodules were formed on peas. This means that the nodulation genes and their products can be analysed in great detail and thus we may understand in precise molecular terms how nodulation occurs.

Map of the cloned nodulation and nitrogen fixation genes of *R. leguminosarum*. The restriction endonuclease sites marked are *EcoRI* (▼), *HindIII* (◆) and *BamHI* (▽). Mutations leading to non-fixing and non-nodulating phenotypes are shown. Regions that hybridise to the nitrogen fixation (*nif*) genes of *Klebsiella pneumoniae* are indicated.

With this information it may be possible to generate strains of *Rhizobium* with an improved symbiotic performance. In addition such studies might have relevance in the analysis of other plant-microbe interactions such as those involving phytopathogens.

Dr A.W.B. Johnston
John Innes Institute
Colney Lane
Norwich
Telephone: (0603) 52571

Phaseolus beans grown with no added nitrogen fertiliser.
Left: no *Rhizobium*.
Centre: infected with partially effective *R. phaseoli*.
Right: infected with highly effective *R. phaseoli*.

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Genetic Manipulation of Crop Plants

CEREAL GENES AND CROP QUALITY

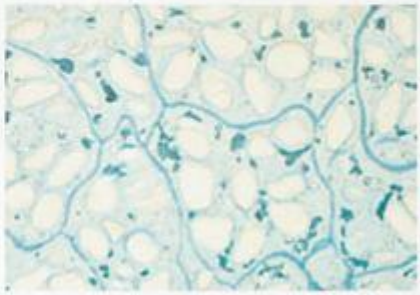
Cereal proteins
This year about twenty million tonnes of wheat and barley grain were harvested in the U.K. The major uses of the grain are in feeding animals and in making bread, biscuits and other flour-based foods. About 10% of the grain is protein, of which half is storage protein. Thus about one million tonnes of this storage protein is produced annually. Besides being the major eventual product of the half a million tonnes of N fertiliser put on cereals these proteins also contribute to the feeding and breadmaking quality of the cereal grains.

Feeding quality
Non-ruminant animals such as pigs and poultry cannot make all of the amino acids that they need and these therefore have to be supplied in the diet. The storage proteins of the cereals are very poor in lysine and threonine; where cereals form the major proportion of the diet they must be supplemented with sources of these amino acids (often imported soyabean meal). Increases in the lysine and threonine content of the cereal grain would decrease the need for such supplementation.

Baking quality
Wheat flour is used for breadmaking because it gives a viscoelastic dough when wetted. The properties of this dough are largely, but not entirely, determined by the protein of the dough which is called gluten. The storage proteins of the grain form the gluten of dough; one particular group called the high molecular weight proteins, appears to be very important in determining breadmaking quality.

The storage proteins in wheat flour, when washed free of starch, form the viscoelastic mass known as gluten.

Gene cloning
Research at Rothamsted Experimental Station and the Plant Breeding Institute, using recombinant DNA technology coupled with the techniques of protein chemistry and genetics, has provided considerable information about these proteins. There are three major groups of storage proteins. Cloned sequences relating to each of these families of genes have been isolated including those for the lysine-poor barley proteins and the high molecular weight proteins thought to be important in making dough elastic. The results show that each group is specified by a family of linked genes and each family of genes (and thus proteins) appears to have been built up from simple repeating structures. The information gained from this detailed study will be used for crop improvement in the future and provide a base for exploiting these proteins in the food industry.



During the development of the endosperm the storage proteins are deposited in protein bodies which (when stained blue) can be seen distributed between the starch grains in the cells of a developing barley seed.

Recombinant DNA techniques have allowed the sequences of the proteins to be deduced; this picture shows the separation of DNA fragments which allows the sequence of nucleic acid bases to be read. It is this sequence of bases that specifies the order of amino acids in the protein and thus eventually determines its properties. In the example shown the results predict a repeating sequence of amino acids that probably makes up a considerable proportion of the high molecular weight gluten proteins.

Mutant barleys

The amino acids lysine and threonine are made by the plant via a synthetic pathway subject to complex regulation. A laboratory selection system, developed, at Rothamsted, has been used to find mutant plants with altered regulation of the pathway. Some of these contain up to fifteen times the normal content of soluble (i.e. non-protein) threonine in their seeds. Two genes are involved and double mutant plants have been produced. Further mutants which also produce extra lysine are being sought. Meanwhile stocks of the high threonine barley have been released to private and state breeders for further evaluation.

Dr B.J. Miflin
Rothamsted Experimental Station
Harpenden, Herts
Telephone: (05827) 63133

The harvested ears and grains of a high threonine barley line (right) are very similar in yield, protein composition and morphology to the control line (left).

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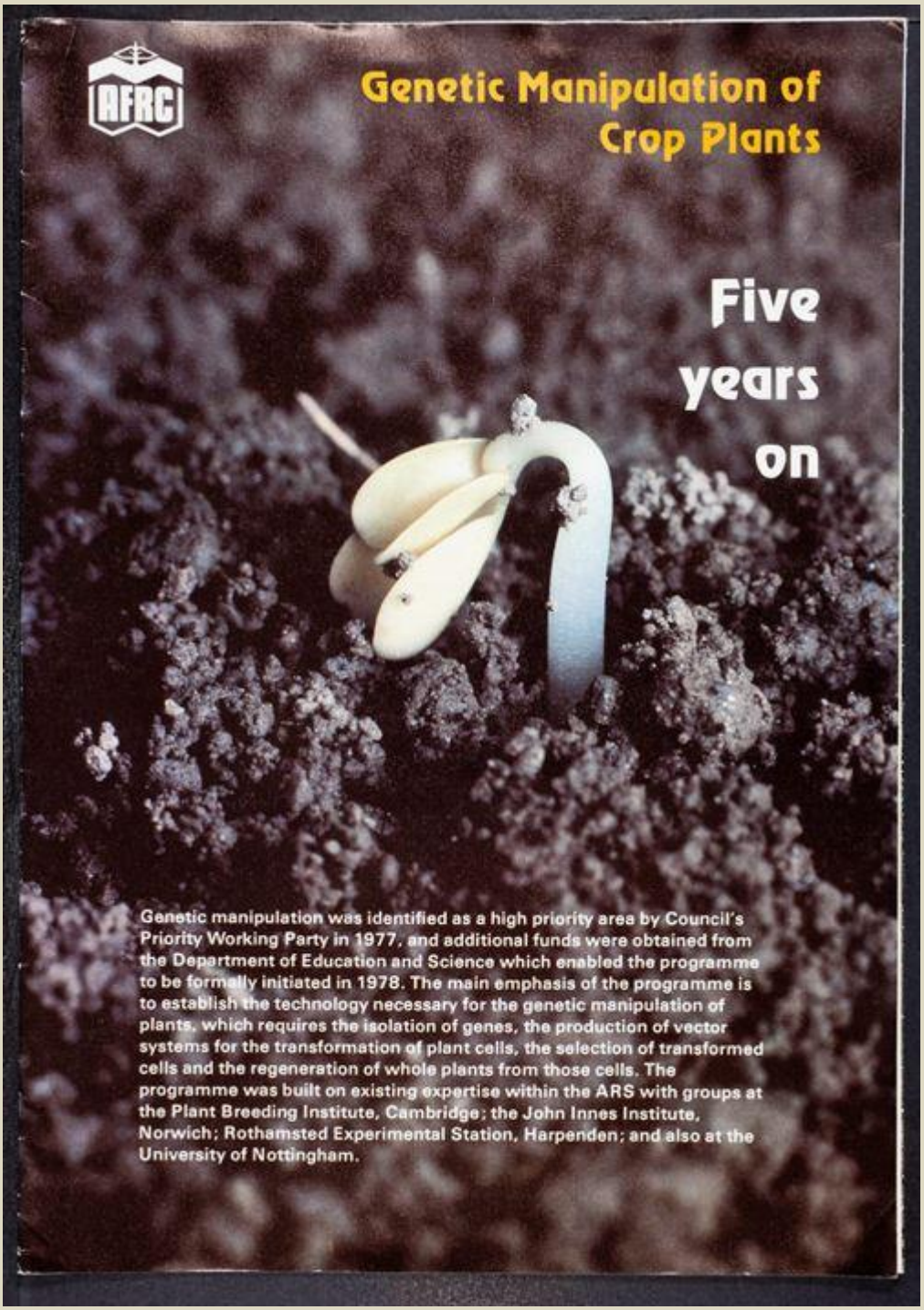
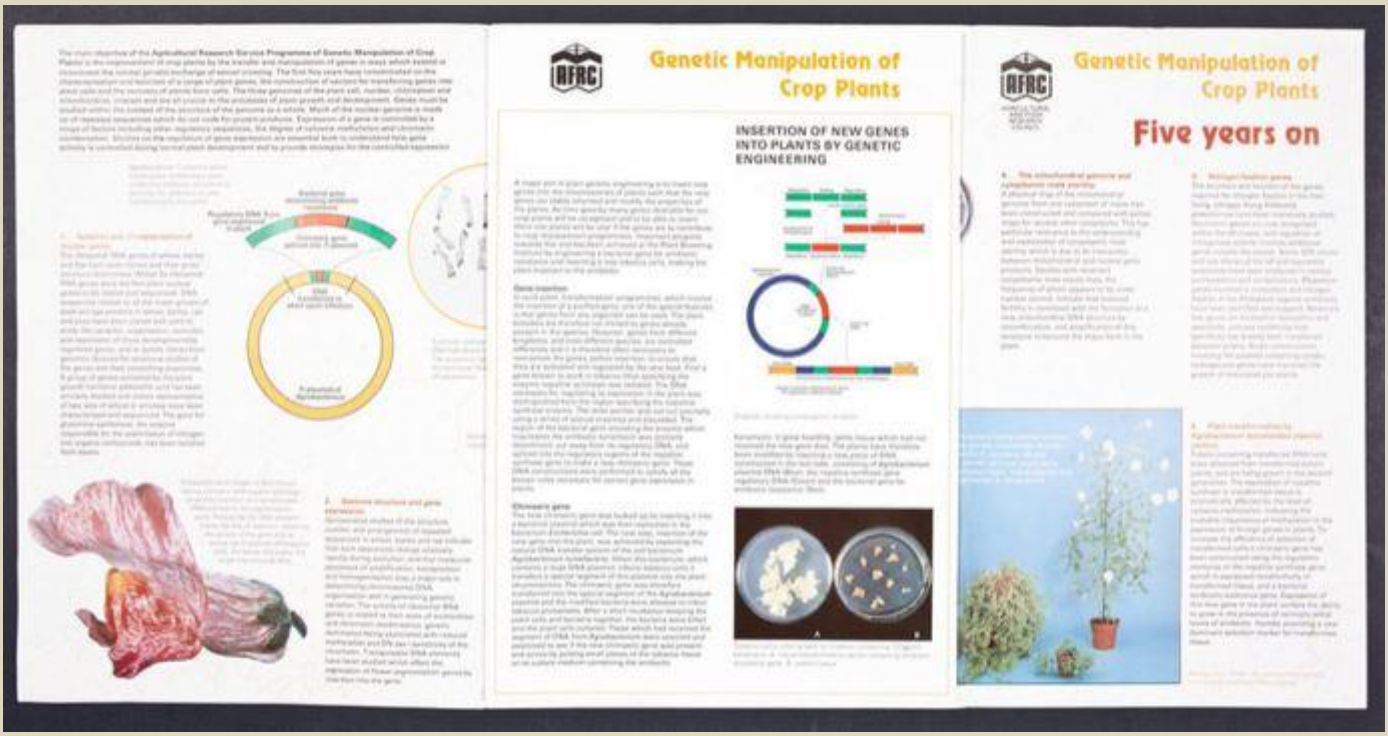
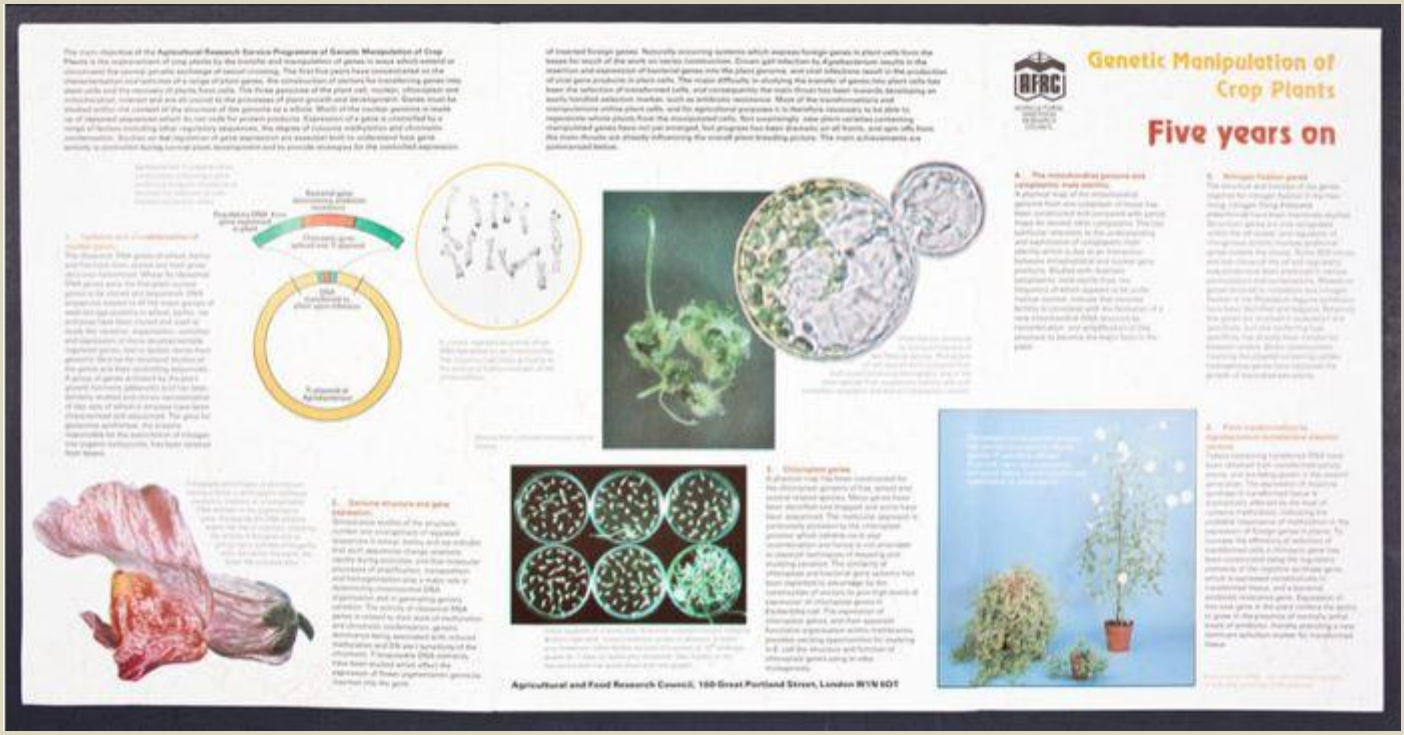
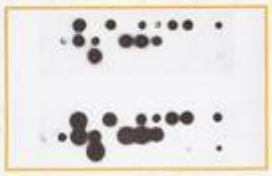

AFRC
Genetic Manipulation of Crop Plants
Five years on
Genetic manipulation was identified as a high priority area by Council's Priority Working Party in 1977, and additional funds were obtained from the Department of Education and Science which enabled the programme to be formally initiated in 1978. The main emphasis of the programme is to establish the technology necessary for the genetic manipulation of plants, which requires the isolation of genes, the production of vector systems for the transformation of plant cells, the selection of transformed cells and the regeneration of whole plants from those cells. The programme was built on existing expertise within the ARS with groups at the Plant Breeding Institute, Cambridge; the John Innes Institute, Norwich; Rothamsted Experimental Station, Harpenden; and also at the University of Nottingham.


Genetic Manipulation of Crop Plants
INSERTION OF NEW GENES INTO PLANTS BY GENETIC ENGINEERING
Genetic Manipulation of Crop Plants
Five years on

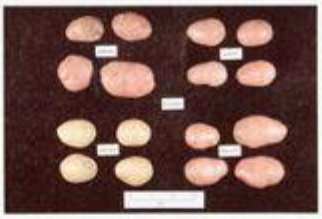

Genetic Manipulation of Crop Plants
Five years on
Agricultural and Food Research Council, 160 Great Portland Street, London W1N 6DT

Genetic Manipulation of Crop Plants

7. Viruses as model genomes and potential vectors.
The DNA genome of cauliflower mosaic virus has been characterised and cloned, the cloned DNA being infective. Non-essential regions of the genome have been identified and deleted to make space for the insertion of foreign genes. Several features of the genome and its transcription are strikingly similar to those of animal tumour viruses which replicate by reverse transcription and of eukaryotic transposable elements, with very significant implications for the study of gene expression and genetic manipulation of plant cells. The complete sequence of the small, single-stranded DNA genome of one gemini virus has been determined, and the genome of maize streak virus, which infects maize, wheat, sugar cane and grasses has been mapped and cloned.



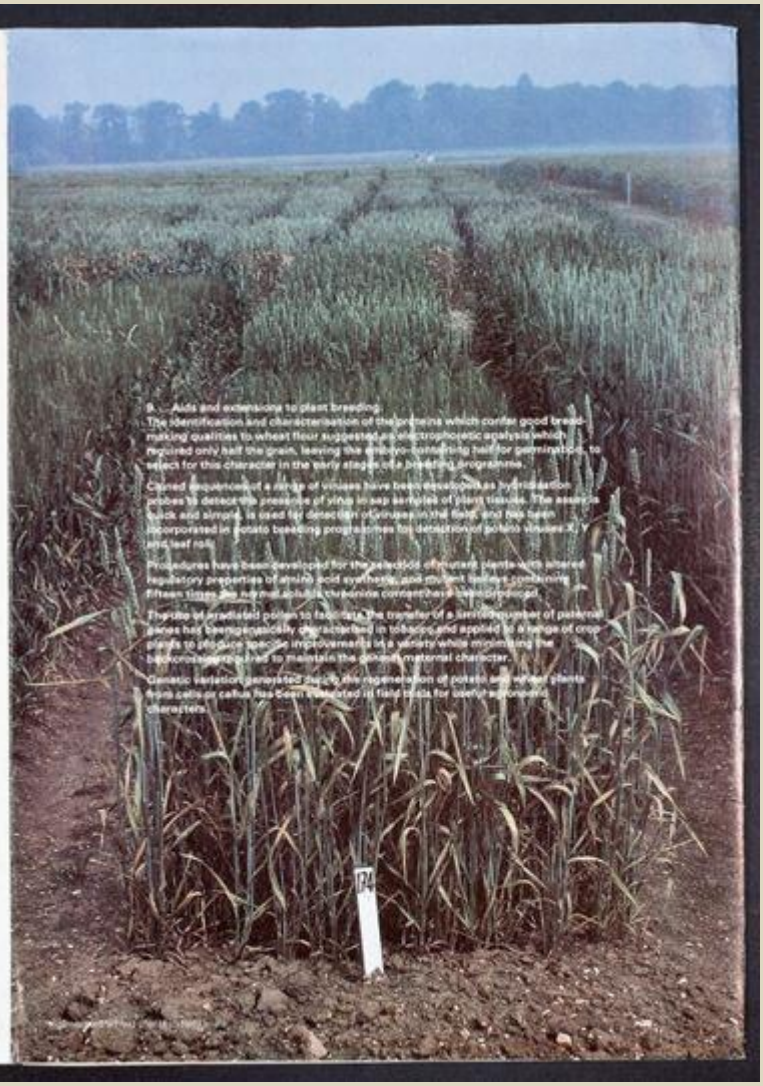
Sap spot test for virus. A cloned probe of DNA from potato leaf virus X was hybridised to spots of sap taken from individual plants in a breeding programme. The size of the spot relates to the level of virus in the sap.



White skinned variant from Desirée plants (normally red skinned tuberal regenerated from tissue culture. The trait is stably expressed through tuber generations.

Protein from wheat seed fractionated by polyacrylamide gel electrophoresis. Wheat varieties show considerable variation in their high molecular weight glutenin subunits (numbered 1 to 12).

8. Plant regeneration and somatic hybrids.
Protoplasts from a range of crop plants including potato, oilseed rape, sugar beet, Italian ryegrass, white clover, red clover, lucerne and sainfoin, and from a variety of horticultural species, can be isolated and induced to divide and grow into callus, and plants have been regenerated from potato, oilseed rape and forage legume protoplasts. Plants can also be regenerated from callus formed on excised tissue from some of the more recalcitrant species, such as cereals. Plants regenerated from either protoplasts or explants of potato, or from explants of wheat, show a range of genetic variation. Somatic hybrid plants between sexually incompatible *Petunia* species have been produced, and somatic cell hybrids between forage legumes have been selected.



9. Aids and extensions to plant breeding.
The identification and characterisation of the proteins which confer good bread-making qualities to wheat flour suggested an electrophoretic analysis which required only half the grain, leaving the embryo-containing half for germination, to select for this character in the early stages of a breeding programme.

Cloned sequences of a range of viruses have been developed as hybridisation probes to detect the presence of virus in sap samples of plant tissues. The assay is quick and simple, is used for detection of viruses in the field, and has been incorporated in potato breeding programmes for detection of potato viruses X, Y and leaf roll.

Procedures have been developed for the selection of mutant plants with altered regulatory properties of amino acid synthesis, and mutant barley containing fifteen times the normal amount of the amino acid lysine has been produced.

Transfer of irradiated pollen to facilitate the transfer of a limited number of paternal genes has been successfully characterised in tobacco and applied to a range of crop plants to produce specific improvements in a variety while minimising the backcrossing required to maintain the genetic maternal character.

Genetic variation generated during the regeneration of potato and wheat plants from cells or callus has been evaluated in field trials for useful agronomic characters.

Genetic Manipulation of Crop Plants

INSERTION OF NEW GENES INTO PLANTS BY GENETIC ENGINEERING

A major aim in plant genetic engineering is to insert new genes into the chromosomes of plants such that the new genes are stably inherited and modify the properties of the plants. As time goes by many genes desirable for our crop plants will be recognised and to be able to insert them into plants will be vital if the genes are to contribute to crop improvement programmes. Important progress towards this end has been achieved at the Plant Breeding Institute by engineering a bacterial gene for antibiotic resistance and inserting it into tobacco cells, making the plant resistant to the antibiotic.

Gene insertion

In such plant 'transformation' programmes, which involve the insertion of a purified gene, one of the special features is that genes from any organism can be used. The plant breeders are therefore not limited to genes already present in the species. However, genes from different kingdoms, and even different species, are controlled differently and it is therefore often necessary to restructure the genes, before insertion, to ensure that they are activated and regulated by the new host. First a gene known to work in tobacco (that specifying the enzyme nopaline synthase) was isolated. The DNA necessary for regulating its expression in the plant was distinguished from the region specifying the nopaline synthase enzyme. The latter portion was cut out precisely using a series of special enzymes and discarded. The region of the bacterial gene encoding the enzyme which inactivates the antibiotic kanamycin was similarly determined, cut away from its regulatory DNA, and spliced into the regulatory regions of the nopaline synthase gene to make a new chimaeric gene. These DNA constructions were performed to satisfy all the known rules necessary for correct gene expression in plants.

Chimaeric gene

The new chimaeric gene was bulked up by inserting it into a bacterial plasmid which was then replicated in the bacterium *Escherichia coli*. The next step, insertion of the new gene into the plant, was achieved by exploiting the natural DNA transfer system of the soil bacterium *Agrobacterium tumefaciens*. When this bacterium, which contains a large DNA plasmid, infects tobacco cells it transfers a special segment of this plasmid into the plant chromosomes. The chimaeric gene was therefore transferred into the special segment of the *Agrobacterium* plasmid and the modified bacteria were allowed to infect tobacco protoplasts. After a short incubation keeping the plant cells and bacteria together, the bacteria were killed and the plant cells cultured. Those which had received the segment of DNA from *Agrobacterium* were selected and examined to see if the new chimaeric gene was present and active by putting small pieces of the tobacco tissue on to culture medium containing the antibiotic

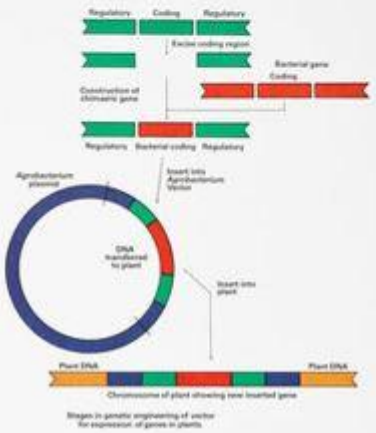
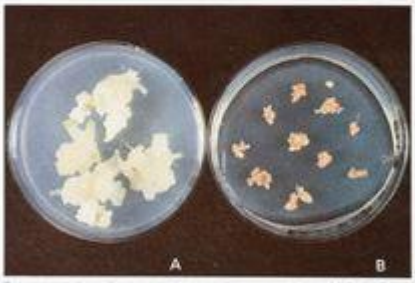


Diagram showing construction of vector

kanamycin. It grew healthily, while tissue which had not received the new gene died. The plants have therefore been modified by inserting a new piece of DNA, constructed in the test tube, consisting of *Agrobacterium* plasmid DNA (Blue), the nopaline synthase gene regulatory DNA (Green) and the bacterial gene for antibiotic resistance (Red).



Tobacco callus after growth on medium containing 120μg/ml kanamycin. A: tissue transformed by vector containing antibiotic resistance gene; B: control tissue

The antibiotic resistance gene inserted into the new plant is not of commercial importance to plant breeders. However, it is a very important gene for future genetic engineering studies in plants because it confers the property of antibiotic resistance to plants, which allows them to be easily selected. Therefore if important genes are attached to the antibiotic genes before insertion, cells possessing the important genes can be selected too.

Construction of modified plants

The transfer of an engineered bacterial gene into plant cells described here, one of the first, opens the door for many similar gene transfers. The construction of modified plants by the insertion of individual genes is now a reality for those species that can be infected by *Agrobacterium*. Much research is being conducted within the ARS to insert new genes into other crop plants to extend the fruits of genetic engineering research to our important crops.

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Genetic Manipulation of Crop Plants

The Plant Genetic Manipulation Group at Nottingham is involved in basic and applied research in the field of somatic hybridization of plants. Part of the programme utilises existing protoplast fusion technology to produce somatic hybrid plants, asymmetric (partial) hybrid plants, and plants exhibiting cytoplasmic exchange (cybrids) for a broad spectrum of genera and species of agronomic and horticultural value. In each of the examples currently under investigation, conventional breeding methods are either inefficient or ineffective in securing species hybridization.

Cell fusion

For certain species of agronomic value, cell fusion techniques are being utilised to produce the somatic hybrid where it can be predicted that novel characteristics may be introduced, or existing traits modified, through hybridization with a related, yet sexually incompatible, species. Such examples include *Lactuca sativa* (lettuce) for resistance to *Bremia*; *Arachis hypogea* (peanut) for leaf spot and mite resistance; *Solanum viarum* for solasidine production; *Lycopersicon esculentum* (tomato) for *Fusarium* wilt resistance; *Trifolium repens* (white clover) and *Medicago sativa* (lucerne) for eliminating the tendency to cause bloat in grazing animals; *Petunia* and other ornamentals in the Solanaceae and Compositae for floral modification and extension of flowering period; and the water fern *Azolla* for increased biomass, temperature tolerance and improved symbiotic nitrogen fixation.

Solanum, Petunia and Nicotiana

Against a taxonomic background, an assessment of the limitations, in practical terms, of somatic hybridization within the Solanaceae, provides the basis for more fundamental investigations aimed at improving the throughput of somatic hybrid material. In this respect studies involve an assessment of electro-fusion of protoplasts, the use of fluorescent labelling techniques and fluorescence-activated cell sorting systems. The merits of producing and utilising double mutants in plants, as compared with single heterokaryon isolation or mass selection procedures, for the recovery of hybrid plants are being evaluated using *Nicotiana* species. Somatic hybrids within the genera *Petunia* and *Nicotiana* provide material for the analysis of nuclear and cytoplasmic interactions and breeding characteristics. Cell fusion techniques are also being utilised to modify plants solely with respect to their cytoplasmic make-up, for example the introduction of cytoplasmic male sterility into *Brassica*.

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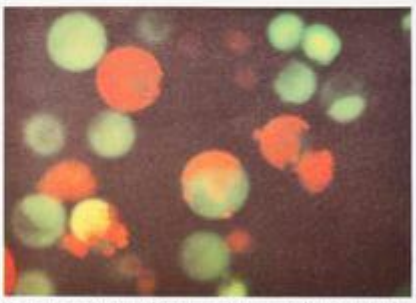
SOMATIC HYBRIDIZATION OF PLANTS



Heterokaryon between *Nicotiana tabacum* and *N. rustica*. Leaf mesophyll protoplasts of *N. tabacum* (fluorescing red under UV light) were fused, using the high pH/Ca^{++} procedure, with fluorescein isothiocyanate (FITC) stained cell suspension protoplasts of *N. rustica* (fluorescing green under UV light). The heterokaryon shows combined chlorophyll and FITC fluorescence.

Protoplasts of a streptomycin resistant and nitrate reductase deficient double mutant of *N. tabacum* were fused with protoplasts of wild type *N. rustica*. Hybrid colonies were selected in medium containing nitrate as sole nitrogen source and also containing streptomycin. Plants were regenerated from these colonies. The floral morphology of hybrid plants (centre) was intermediate between *N. rustica* (left) and *N. tabacum* (right). *N. rustica* has a gene for black ovary wall, and the somatic hybrid also possesses this dominant gene and has a black ovary wall.

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Genetic Manipulation of Crop Plants

PLANT CULTURE AND CROP IMPROVEMENT

One of the major aims of the ARS programme on Plant Genetic Manipulation is to produce new methods for generating and transferring useful agronomic characters in addition to those normally used in plant breeding. Plant cells will divide and grow in culture either from individual protoplasts (naked cells) or from pieces of tissue. In many species whole plants can be regenerated from protoplasts or tissue cultures by suitable manipulation. The use of such cell culture techniques provides several potential opportunities for achieving this aim by (1) using the rearrangement of existing genetic material that occurs spontaneously during plant regeneration ('somaclonal variation'), (2) transformation of plant cells by specific DNA vectors leading to the incorporation of particular 'foreign' genes, (3) transfer of multi-gene characters via protoplast fusion. Examples of successes with the first two techniques are given below.

Somaclonal variation in wheat and potato

At Rothamsted, immature embryos of wheat have been induced to form tissue cultures from which many hundreds of plants have been regenerated. These plants have been assessed in field trials and variation in height, date of flowering and maturity, presence or absence of awns, yield, thousand grain weight and seed storage proteins have been observed. Some, but not all, of this somaclonal variation arises from identified changes to the chromosomes. Some of the regenerant lines have been selected for further trials by private breeders. This approach may lead to production of new variations of established wheat cultivars.

Regenerated wheat plants in field trials

Regenerated potato plants in field trials

Plants have been regenerated from tissue cultures derived from leaf, rachis and stem pieces of potato, and from protoplasts of ten British and European potato cultivars. As with wheat, plants regenerated from tissue cultures are not all identical to the parental material, and vary in many characters including yield, tuber shape and tuber colour. Chromosome numbers of plants originating from protoplasts are more variable than those originating from cultured tissues. Chromosomally normal plants with properties differing from parental cells have been obtained, and regenerated plants have been evaluated in field trials. The importance of these techniques (including protoplast fusion) for potato is that they will allow the alteration or upgrading of existing potato cultivars, which is difficult by conventional breeding.

Freshly isolated potato protoplasts

Sprouting tuber and growing plant of a transformed potato

Transformation of potato

The most successful technique at present for the delivery of specific 'foreign' genes into single plant cells makes use of the soil bacterium *Agrobacterium tumefaciens*. Using this bacterium several laboratories have obtained transformed plants of tobacco and petunia. At Rothamsted, potato cells have been transformed and full sized plants regenerated which have readily produced tubers. When one of these tubers was taken and sprouted it produced roots and shoots. The introduced genes were still present and were expressed. This is the first example in the U.K., and probably in the world, of the transformation of a major food crop in which foreign genes have been inserted and carried through to the next (vegetative) 'generation'.

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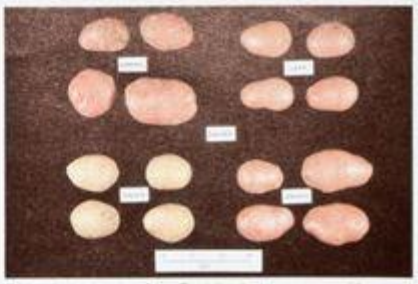

White skinned variant from Desirée plants regenerated from tissue culture. The trait is stably expressed through tuber generations.

Chromosomes of root cell protoplast-derived potato plant (cv. Majestic). Normal chromosome number, but with a translocation resulting in one large and one small chromosome (arrows).

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Genetic Manipulation of Crop Plants

CAULIFLOWER MOSAIC VIRUS

Cauliflower mosaic virus (CaMV) is a plant virus containing double-stranded, circular DNA. The molecular biology of this and other DNA viruses of plants is being investigated in the Virus Research Department at the John Innes Institute. The aims are:

a) to understand the molecular pathology of virus-plant interaction, to provide fundamental information which could lead to methods for disease control.

b) to study the replication of the DNA and its gene expression, as a model system adapted to plant cells; an approach to understanding more about plant genes.

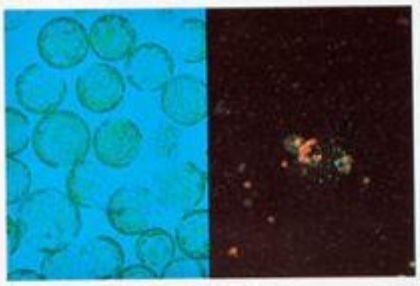
c) to investigate means of using viral DNA as plant gene vectors by identifying DNA control sequences that might be used to construct such vectors; and to remove non-essential genes, such as an aphid transmission factor gene and study the consequences of replacing this with foreign DNA such as synthetic oligomers, selection markers and plant, bacterial, or animal genes.

CaMV DNA genome showing the *Bst*EII–*Xho*I region, associated with aphid transmission, in red. The gold shadowed scanning E.M. is of *Myzus persicae*.

CaMV is normally transmitted by the aphid *Myzus persicae*. This function is impaired in the isolate 'Campbell', and *in vitro* construction of hybrid molecules between cloned DNA of Cabb B–JI (aphid transmissible) and Campbell (aphid non-transmissible) shows that the aphid transmission depends upon the DNA between *Bst*EII and *Xho*I restriction enzyme sites.

Deletion mutations in the small gene (II) partially within the *Bst*EII–*Xho*I region also eliminate aphid transmission, but the virus is still viable, and plants infected with gene II deletion mutant (Δ 5) develop normal disease symptoms. Gene II is therefore non-essential.

A turnip plant showing CaMV symptoms, particularly vein 'clearing', on a young leaf. Infection was with Δ 5, a gene II deletion mutant which is infectious but not aphid transmissible.



Turnip protoplasts (left); protoplasts showing immunofluorescent staining to demonstrate CaMV infection (right).

To study the replication of CaMV DNA, a 'single-cell' protoplast system has been developed. Ultimately, introduction of viral DNA vectors into protoplasts that can regenerate to plants is an ideal step in transferring foreign genes into plants.

Foreign DNA is inserted into a non-essential region of CaMV DNA cloned in a bacterial plasmid. The CaMV DNA is excised and introduced into protoplasts or inoculated on to plants. Current studies involve the problems of instability of newly introduced DNA sequences and foreign genes in plants.

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THE AGRICULTURAL GENETICS COMPANY

Biotechnology is currently one of the most rapidly developing and exciting areas of science and is likely to produce a wide range of new industries in the future. The Agricultural and Food Research Council was one of the first organisations to recognise the potential of this new technology and five years ago launched a major programme of research into the genetic manipulation of crop plants. This intense effort has led to considerable increases in the knowledge and understanding of the sciences associated with biotechnology.

Technology Transfer

Recently it became clear that there was no established means of exploiting this new knowledge and to meet this need the Agricultural Genetics Company was formed in July 1983. The role of the Company is to act as the technology transfer organisation undertaking commercial development of appropriate plant science based work from certain Agricultural Research Service institutes and collaborating universities. This includes the areas in which they excel, notably non-conventional plant breeding, microbial inoculants and biological control products.

The Agricultural Genetics Company was founded by the British Technology Group, who have already made a major investment in biotechnology, and two private investors, Ultramar and Advent.

Ultramar is a British-owned independent oil company with a turnover of £1.4 billion derived from large-scale refining and marketing interests in Canada and US and with North Sea involvement. Their support for the Agricultural Genetics Company is their first investment in agriculture.

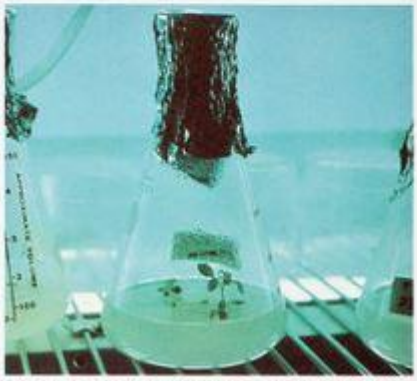
For Advent, the Agricultural Genetics Company represents a further association in line with their main-stream activities aimed at investment in high technology, high growth sectors at an early stage in their development.

The Company is expecting to develop to an initial capital base of £15m which will be provided by the founding shareholders and new private sector investors.

Trial plots of new cereal varieties at the Plant Breeding Institute, Cambridge.

Research programme

Under a collaborative agreement the Agricultural Genetics Company and the Agricultural and Food Research Council will carry out specific joint research projects for which world-wide marketing opportunities are seen. Its efforts will not be restricted to the public sector and the Agricultural Genetics Company will also seek to work with private sector research, either as a customer or contractor.



Regeneration of plants in the laboratory using tissue culture techniques.

The Agricultural Genetics Company will also have an Advisory Panel composed of eminent agriculturalists, scientists and others. Its role will be to comment on specific areas of activity, suggest, and advise on new areas for investigation and development. The Company will initially have a small, highly qualified staff whose efforts will be focussed on applied research, marketing and the development of commercial joint ventures with established agro-industrial companies.

The Directors of the Agricultural Genetics Company are:

Dr Alan Robertson, Chairman
Dr Roger Gilmour, Chief Executive
Dr Ralph Riley FRS
Mr Christopher Stott FCA
Mr David Cooksey
Mr David Elton
Dr James Cain

The Agricultural Genetics Company has been formed with the agreement of the Departments of Education and Science, Trade and Industry and the Ministry of Agriculture.

For further information about the Agricultural Genetics Company please contact Dr R.H. Gilmour, Chief Executive or P.R. Hayward, Marketing Projects Manager.

The Agricultural Genetics Company Limited, 27-28 Bridge Street, Cambridge CB2 1UJ. Telephone: (0223) 312882.

https://aim4truth.org/2020/05/07/the-british-rothschild-biowarfare-conspiracy/