



SCIENCE BULLETIN

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Physicists from the R.O.C. Join in the Top Quark Search at Fermilab

The quest for the fundamental building blocks of matter has attracted the attention of scientists for centuries. According to theoretical models, all matter consists of leptons and quarks, which come in three families. By now, most of the predicted elementary particles have been found. However, the search for the top quark, the last and heaviest, has been underway ever since the discovery of the bottom quark 17 years ago. This has turned out to be one of the greatest challenges ever faced by particle physicists.

In a recent press conference, the

CDF Collaboration at the Fermi National Accelerator Laboratory in Chicago, Illinois announced the first "Evidence of Top Quark Production." Although statistics are limited, this could be the biggest breakthrough in high energy physics in recent years. The results of this top search have been submitted to *The Physical Review* for publication. Four physicists from the Academia Sinica in the Republic of China are listed as co-authors of the paper.

The CDF Collaboration currently consists of over 440 physicists from 36 institutions in the United States,

Italy, Japan, Canada, and Taiwan. The Taiwan members, from the Institute of Physics at the Academia Sinica, officially joined the CDF Collaboration in March 1993. Since then, under the coordination of Dr. G. P. Yeh, leader of the top dilepton search group at the CDF, the Taiwan group has made visible contributions to the CDF experiment, concentrating most of its efforts on projects dealing with both hardware and software related to the silicon microstrip detector.

This international collaboration effort has received strong support from the National Science Council of the R.O.C.

Animal Models of Human Diseases in Taiwan

According to *The Annual Report of Health and Vital Statistics, 1989-1993* of the Department of Health, Executive Yuan, the ten leading causes of death in Taiwan are: cancer, central nervous vascular disease, accident and abnormal social, psychological behavior, cardiovascular diseases, diabetes mellitus, chronic hepatopathy and cirrhosis, pneumonia, hypertension, bronchitis, emphysema and asthma, and nephritis, nephropathy and nephrotic syndrome. (Table 1)

One of the purposes of the National Laboratory Animal Breeding and Research Center of the National Science Council is to develop, and breed animals with different genetic characteristics for human disease study and biomedical research. (Table 2)

By research object and function, the animal models are basically categorized as experimental, spontane-

ous, negative or orphan.

(A) Experimental models

The researcher tries to reproduce a disease process found in the target or laboratory animal species of interest. These models can precisely manipulate variable factors - dose, route of administration, and exposure schedule.

These models have great application in research designed to determine the disease potential of concurrent exposure to more than one type of infectious or toxic agent. These models also permit a means of controlling an animal's physical environment to simulate that of the target species.

(B) Spontaneous models

These models are those that occur naturally, and are therefore not induced through intervention by the researcher. In order for a disease to

be recognised, knowledge of its pathogenesis in the model and target animal species is necessary.

Spontaneous models typically reveal similarities, but do not exactly mimic counterpart conditions in the target species. The value of these models is in providing interspecies comparisons and clues to disease causation.

(C) Negative models

These models represent the normal counterpart of the diseased animal.

(D) Orphan models

An orphan model is a disease existing in a model animal species, when no apparent counterpart is recognised in the target species. For example, slow virus infection such as Visna and Scrapie were first recognised in sheep. Later, the counterpart spongiform encephalopathy conditions of Kuru and Creutzfeldt

Table 1 The Top Ten Causes of Death in Taiwan from 1989 to 1993

	Rank					Number of Deaths					Mortality Percentage				
	'89	'90	'91	'92	'93	'89	'90	'91	'92	'93	'89	'90	'91	'92	'93
Cancer	1	1	1	1	1	18,878	18,536	19,630	20,959	22,291	18.46	17.81	18.79	19.26	20.44
Central Nervous Vascular Disease	2	2	2	2	2	14,461	14,174	14,137	14,325	13,666	14.14	13.62	13.53	13.17	12.53
Accident and Abnormal Social/Psychological Behavior	3	3	3	3	3	14,047	13,928	13,636	13,152	13,239	13.74	13.38	13.05	12.09	12.14
Cardiovascular Disease	4	4	4	4	4	10,699	11,505	12,026	12,993	12,483	10.46	11.05	11.51	11.94	11.45
Diabetes Mellitus	5	5	5	5	5	3,868	3,960	4,210	4,887	5,365	3.78	3.80	4.03	4.49	4.92
Chronic Hepatopathy and Cirrhosis	6	6	6	6	6	3,550	3,606	3,601	3,748	3,753	3.47	3.46	3.45	3.44	3.44
Pneumonia	7	7	7	8	8	2,996	3,358	2,644	2,907	2,812	2.90	3.23	2.53	2.67	2.58
Hypertension	8	8	9	9	9	2,946	2,993	2,492	2,300	2,281	2.88	2.88	2.38	2.11	2.09
Bronchitis, Emphysema and Asthma	9	9	10	10	10	2,551	2,478	2,176	2,085	1,852	2.50	2.38	2.08	1.92	1.70
Nephritis, Nephropathy and Nephrotic Syndrome	10	10	8	7	7	2,094	2,304	2,527	2,935	2,856	2.05	2.21	2.42	2.70	2.62
Total Causes of Death						102,242	104,089	104,461	108,810	109,069	100	100	100	100	100

Adapted from *Annual Report of Health and Vital Statistics 1989-1993*, Department of Health, Executive Yuan

Table 2 Animal Models of Human Diseases Supplied by the National Laboratory Animal Breeding and Research Center

Human disease	Animal Models
Mice	
M ammary gland Cancer	C3H/HeN
Leukemia	AKR
Pulmonary Cancer	BALB/c
Hepatic Cancer	C57BL/6N, CBA
Amyloidosis	A/HeN
Autoimmunity	NZW/N
Cheiloschisis	A/HeN
Hydrocephalus	C57BL/6N
Immuno T cells Deficiency	Nude Mice
Polyarteritis Nodosa	DBA/2N
Rats	
Hypertension	SHR/N
Diabetes Mellitus	B.B.
Arthritis	S.D.
Obesity	Obese
Colorectal Cancer	Wistar
Interstitial Cell Tumor in testis	F344/N
Hamsters	
Cancer cell Implantation	G.B.
Periodontal disease	G.G.
Guinea Pigs	
Scurvy	DH
Malignant Melanoma	2/N
Tuberculosis	13/H

–Jakob disease were recognised as slow virus diseases that occur in people.

The top ten human diseases in Taiwan and related animal models are outlined as follows:

I. Cancer:

In the past five years (1989 to 1993), cancer has been the most common killer in Taiwan. Last year, about 4,300 peoples died of hepatic cancer. The predisposed factors include B&C type hepatitis, chronic hepatitis and cirrhotic patients. Lung cancer is another killer which has increased dramatically. The causes include smoking and air pollution.

Other cancers, for examples – nasopharyngeal cancer (NPC), mammary gland tumor, malignant lymphoma, leukemia, brain cancer, genital cancer, gallbladder cancer, and colorectal cancer are the most common cancers found in the people of Taiwan. The animal models used for cancer study are dogs, ducks, mice, etc.

II. Central nervous vascular disease:

Atherosclerosis, probably the most prevalent and important form of vascular disease in humans, affects large- and medium-sized arteries. Involvement of cerebral arteries leads to cerebral infarcts.

In addition, the affected arteries are prone to aneurysms that may

rupture. Cerebral vascular disease is the second leading cause of death and disability in Taiwan.

Models used include rats, rabbits, birds, pigs, nonhuman primates, and dogs.

The lesions can be produced by feeding an atherogenic or hypercholesterolemic diet to the animals, resulting in occlusive atherosclerotic coronary disease, myocardial infarcts or/and cerebral infarcts.

III. Accident and abnormal social / psychological behavior:

The third leading cause of death is accident – e.g. abuse of drugs, murder, car accidents, airplane accidents, fire, and drowning. It is possible to decrease accidental death by social pressure and law. It is not easy to find an animal model for this category.

IV. Cardiovascular disease:

The fourth leading cause of death in Taiwan is cardiovascular disease.

Myocardial infarction associated with coronary arteries atherosclerosis and cardiomyopathies are major and common causes of heart failure and death.

Cardiomyopathies may be divided into (a) primary, which is not associated with a systemic disease and is of unknown cause, and (b) secondary, part of a generalized disease

The primary form of cardiomyop-

athy may be classified, on the basis of pathophysiological observation, as hypertrophic, especially of the interventricular septum, with or without ventricular outflow tract obstruction; congestive with cardiac dilatation, congestive heart failure, insufficiency of mitral and tricuspid valves; or restrictive, due to endocardial fibrosis. These types are not always clearly identifiable, as one type may progress to another.

The animal models include Syrian hamsters, rats mellitus and turkeys.

V. Diabetes mellitus:

The fifth leading causes of death. Diabetes may be divided into two major types: (a) juvenile-onset, ketosis-prone, insulin-dependent, hypoinsulinemia and (b) maturity-onset, nonketotic, non-insulin-dependent, obesity.

The models for hypoinsulinemia are BB rats (spontaneous mutation of the Wistar rat). – 30% of the rats develop absolute insulin deficiency between 60 and 120 days of age with clinical signs of hypoinsulinemia, hyperglycemia and ketosis.

Other animal models include Chinese hamsters (*Cricetulus griseus*), South African hamsters (*Mystromys albicaudatus*), New Zealand white rabbits, etc. The most frequent cause of spontaneous diabetes in dogs is chronic pancreatitis in which there is progressive loss of both exocrine and endocrine cells by inflammatory destruction and fibrosis. Spontaneous cases of diabetes in domestic cats and nonhuman primates are associated with amyloid deposits in the islets of Langerhans.

Experimentally, alloxan, streptozotocin and inoculation of encephalomyocarditis virus can cause hypoinsulinemia in mice.

Animals with hyperinsulinemia are common among obese laboratory rodents. Although the precise metabolic defects are not understood completely, diabetes in most of the animal species listed below is associated with either hyperplastic or hypertrophic changes in the beta cells of the islets of Langerhans. The animal models include spiny, KK, C3Hf x 1, obese, diabetes, PBB and New Zealand obese mice, etc.

VI. Chronic hepatopathy and cirrhosis:

The sixth leading cause of death in Taiwan. Approximately 4,000 cases of hepatic cancer were found last year, three fourths with cirrho-

sis; one fourth was related to C-type hepatitis. C type hepatitis cases are the major category of hepatopathy in Japan; in contrast, B type hepatitis tends to be epidemic in the Taiwan area.

VII. Pneumonia

Respiratory tract infections are more frequent than infections of any other organ and account for the greatest number of workdays lost in the general population.

The vast majority are upper respiratory tract infections caused by viruses. But viral, mycoplasmal, bacterial, and fungal infections of the lung (pneumonia, bronchopneumonias, lung abscesses) still account for an enormous amount of morbidity and rank among the major causes of death.

Pneumonia is the seventh leading cause of death in Taiwan.

The animal models include dogs, cattle, horses, guinea pigs, and rats.

VIII. Hypertension:

Hypertension is defined as sustained elevation of blood pressure above accepted normal values. Hypertension is classified as (a) primary and (b) secondary. Over 90% of human cases are of the primary type. Secondary hypertension is associated with a variety of causes, including renal, endocrine, neurologic, and vascular disorders. The most commonly used model is spontaneously hypertensive rats (SHR), with hypertensive lesions developing spontaneously in 100% of the offspring several months following birth. Other models include mice, chickens, rabbits, dogs and horses.

IX. Bronchitis, Emphysema and Asthma:

Chronic bronchitis in man has an imperceptible onset and insidious progress over a period of years. By the time it is recognized clinically, it is manifested by persistent coughing and sputum production and a pattern of acute exacerbations.

The animal models include dogs and horses.

Asthma is a relatively common

condition in man and estimated to occur in 5% of all children. The models include dogs and cats.

Emphysema in humans may be subdivided into (a) panlobular or panacinar, affecting all alveolar ducts and alveolar sacs in a unit - e.g. rabbit models, usually after 2½ years of age. (b) centrilobular or proximal acinar, affecting mainly respiratory bronchioles with subsequent extension and involvement of the alveoli, (c) paraseptal or distal acinar, involving the subpleural tissue and interlobular septa, and (d) irregular or paracicatricial, involving secondary lobules, usually with scarring - e.g. rat models.

The other animal models include cattle, horses, dogs, and mice.

This category is the ninth leading cause of death in Taiwan.

X. Nephritis, nephropathy and nephrotic syndrome:

These causes of death have increased dramatically recently.

Certain glomerular diseases (membranous GN, lipoid nephrosis, focal sclerosis) virtually always produce the nephrotic syndrome (NS). NS has the following features: (a) massive proteinuria with the daily loss of 3.5 gm or more of protein. (b) hypoalbuminemia with plasma albumin levels less than 3gm per dl (c) Generalized edema (d) hyperlipidemia.

Glomerulonephritis constitutes another important part of human renal disease. Primary glomerulonephritis represents a glomerular disease in which the kidney is the only or predominant organ affected. Secondary glomerulonephritis represents a glomerular disease in which glomeruli may be injured by a variety of factors and in the course of a number of systemic diseases.

In animals, glomerulonephritis is believed to be mediated as an immunologic function of persistent viremia with the formation of antiviral antibodies and subsequent glomerular deposition of circulating immune complexes. The animal models include New Zealand mice (NZBxNZW) F₁ hybrids, dogs with SLE,

diabetic KK mice, Chinese hamsters, Brattleboro rats etc.

Animal models of human disease play an important role in biomedical research and human life. Recently, acquired immune-deficiency syndrome (AIDS) has become a plague of the 20th century. Treatment of this disease also relies upon research with animal models. The National Laboratory Animal Breeding and Research Center confidently develops and breeds animal models of human disease, to supply the SPF (Specific Pathogen Free) high quality animals for biomedical research in Taiwan. (by Chung-Tiang Liang)

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