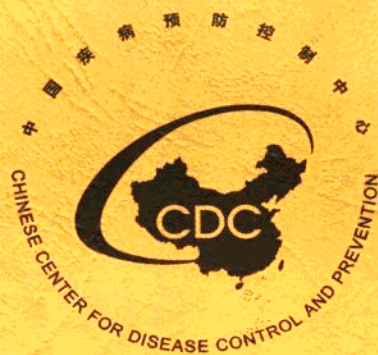


中国疾病预防控制中心年报

ANNUAL REPORT

CHINESE CENTER FOR DISEASE CONTROL AND PREVENTION

(2003)



中国疾病预防控制中心

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序 言

在中国疾病预防控制中心领导的重视和各所科研处、信息部门的支持下，中国疾病预防控制中心公共卫生监测与信息服务中心组织编辑出版中国疾病预防控制中心 2003 年度年报。本年报收集获奖科技成果(中英文对照)、中文学术期刊论文、英文学术期刊论文、主编或参编的中外文书籍。从我们编辑的资料中我们可以看到中国疾病预防控制中心整体的科研水平和反映中国疾病预防控制中心的良好的学术氛围。同时，我们对中心直属单位和非法人独立单位及中心挂靠单位的获奖科技成果、中文学术期刊论文、英文学术期刊论文、主编或参编的中外文书籍进行统计，并制作成分布一览表。希望对疾病预防与公共卫生领域事业的发展起到良好的促进作用。

在此，对中国疾病预防控制中心的直属单位和非法人独立单位及中心挂靠单位对年报资料收集所付出的辛勤劳动表示衷心的感谢！祝愿各单位各项工作取得更大的成绩。

中国疾病预防控制中心公共卫生监测与信息服务中心

2004 年 6 月 20 日

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获奖科技成果

痢疾杆菌全基因组序列测定和分析

- 1、中国疾病预防控制中心病毒病防治所病毒基因工程国家重点实验室
- 2、复旦大学医学院卫生部医学分子病毒学重点实验室
- 3、中国疾病预防控制中心传染病预防控制所卫生部分子细菌学重点实验室
- 4、北京大学人民医院肝病研究所
- 5、国家人类基因组北方研究中心（北京诺塞基因组研究中心有限公司）
- 6、华北制药集团有限责任公司

本项目属于医学微生物学领域的基础研究。

痢疾杆菌福氏 2a 志贺氏菌（简称 Sf2a 301）基因组研究是我国第一个向国际公布并率先完成的微生物基因组计划（环型染色体和毒力大质粒在 Genbank 中的序列编号为 AE005674 和 AF386526）。

本项目全面优化了文库构建和整体测序策略，文库包括 4 万多个克隆，测定了 30 多兆序列，完成全基因组序列测定和分析。通过功能注释与比较基因组学研究，共获得 500 多个新基因，其中近 200 个至今尚未见报道。

Sf2a 301 新基因通过结构模拟和功能预测共获得了数十个编码外膜蛋白的基因，可以作为有效免疫组分和新的药物靶位的候选蛋白，为研制疫苗，实现有效防治奠定坚实基础。Sf2a 301 是目前已知含 IS 序列最多的微生物，提示其基因组异常活跃；与大肠杆菌 K-12MG1655 及 EDL933 菌株的基因组比较后发现，Sf2a 301 的染色体上存在多个大片段的倒置和易位，可能影响细菌的侵袭与致病性；

在染色体上发现许多“基因组岛”。鉴别了 9 个可能的毒力岛，其中 7 个为国际上首次报道；本项目在国际第一次展示了福氏志贺氏菌、大肠杆菌 K-12 以及 O157:H7 的全基因组比较图，从进化角度推测了三者的亲缘关系。Sf2a 301 基因组图是痢疾杆菌四群和 47 个血清型中完成的第一个全基因组精确图，推动了国内微生物基因组学的发展，同时带动了其他相关产业的发展。在北京市科委的支持下，我们开展了痢疾杆菌的蛋白质组学、单基因突变体库和生物芯片的研究。后续功能基因组的开展将进一步确立我国在国际相关研究领域的领先地位。

痢疾杆菌基因组测序的完成及功能基因组研究的开展将从分子水平阐明其致病机理和耐药机制，而药物新靶位、毒力及抗原相关基因的发现以及由此可能研制的新型痢疾疫苗将实现对痢疾的有效防治，市场前景广大，可望产生极大的经济效益。

（荣获 2003 年中华医学科技进步一等奖、2003 年北京市科技进步二等奖）

SEQUENCING AND ANALYSIS OF THE WHOLE GENOME OF *Shigella flexneri* 2a

State Key Laboratory for Molecular Virology and Genetic Engineering
Laboratory of Molecular Virology, Fudan University
Institute of Epidemiology and Microbiology
Hepatology Institute, People's Hospital, Peking University

The project "sequencing and analysis of the whole genome of *shigella flexneri* 2a" is the basic research in medical microbiology field.

Genomic research on *Shigella flexneri* 2a (Sf2a 301) is the first one which our country issued to the world and accomplished before foreign counterpart (accession number of chromosome and virulence plasmid is AE0005674 and AF386526 in GenBank, respectively).

We comprehensively optimized both technology for library construction and strategy for whole genome sequencing. At the same time, we constructed more than 40 thousand genome fragment clones in all and sequenced over 30Mb fragments including the sequence of virulence plasmid. In addition, there predicted over 500 new genes in Sf2a 301 chromosome by the means of functional annotation and comparative genome research, amongst which about 200 genes have not been published.

Several dozens of candidate genes coding outer membrane proteins (OMPs) were proposed by structure simulation and function prediction amongst all new proposed genes of Sf2a 301, whose expression products could act as efficient immuno-components or new target sites for drug therapy. When to functionally annotate its genome, we found Sf2a 301 was one of the most IS-rich microbes, which indicates that its genome is very dynamic. Comparison both with the *E.coli* K-12 MG1655 and EDL933 genome by the means of comparative genomic analysis, there are many large segment inversions and translocations in Sf2a 301 chromosome, which will probably influence the change of its invasion and pathogenicity pattern.

There are many genome islands in its chromosome. We predicated nine likely virulence islands from it, among which seven ones are brand-new. It is the first time to show the comparative genome map between *shigella flexneri*, *E.coli* K-12 and O157:H7. The alignments reveal that *S.flexneri* is more closely related to the non-pathogenic K12 rather than the pathogenic O157:H7. The whole genome map of Sf2a 301 is the first precise map amongst all four groups and 47 serotypes of *shigella* spp.. It pushed on the development of domestic microbial genome research, at the same time accelerated the development of other correlative domestic industries. Currently we are carrying on studies supported by Beijing City such as *shigella* proteome analysis, construction of single gene mutant laboratory and biochip, etc., What involved is most advanced experimental technology or field at present. Undoubtedly following functional genome research will redound to consolidating our country's leading place in the related international field.

With the completion of *shigella* genome sequencing and further functional analysis on its genome, there would advance the exploration of genetic basis which will make us know the mechanism of its pathogenicity and drug resistance better. On the other hand, it makes possible to develop novel vaccine against shigellosis and to find new target sites of drug and candidate genes of virulence and antigen. Moreover, these findings will help to provide the effective prevention and cure for the shigellosis, which will likely produce great economic benefits and have vast potential market prospects.

(Won the First Prize of Chinese Medical Association for Science and Technology, and
the Second Prize for Beijing Science and Technology)

肠出血性大肠杆菌 O157:H7 的流行病学调查和控制措施研究

中国疾病预防控制中心传染病预防控制所

本项目是对我国发生的不明原因疫情的细菌学、临床、血清学和流行病学调查, 以及

将病原明确为肠出血性大肠杆菌 O157:H7 (Enterohemorrhagic *Escherichia coli* O157:H7, EHEC O157:H7) 感染后, 针对现场发现的问题, 开展了深入的流行病学调查和研究, 并将研究成果, 用于指导现场工作, 为我国 EHEC O157:H7 的预防和控制, 提供了新的方法、思路、措施和策略。

首先, 鉴于我国 EHEC O157:H7 感染的爆发和国外报道的流行病学特点不同, 提出假设: 携带病原菌的家畜家禽是传染源, 通过不断排泄粪便等方式, 严重污染环境; 携带病原菌的苍蝇和污染的肉类、腌菜等, 有传播病原菌的作用; 不良家庭卫生和个人卫生状况, 使病原菌得以通过消化道进入人体, 发生疾病。

使用细菌染色体 XbaI 酶切片脉冲场凝胶电泳 (pulsed field gene electrophoresis, PFGE) 方法, 使用 BioNumerics 软件分析 PFGE 图像, 将我国分离的 EHEC O157:H7 菌株, 分成 27 个 PFGE 型, 初步建立了中国大肠杆菌 157 菌株的 PulseNet 资料库, 可用于流行病学调查、传染源和传播途径的追踪。PFGE 分型结果支持家畜家禽是传染源、污染的肉类、腌菜、苍蝇等传播病原菌的假设, 患者菌株和羊鸡猪牛、以及苍蝇等分离菌株属于一个型别, 100%同源; 并首次从蜚蠊分离到 EHEC O157:H7, 提示环境污染严重。对苏皖豫地区持续 4 年的调查发现, 家畜家禽带菌率的高低和疫情发生有相关性。使用志贺毒素 2 基因分型方法发现, 从 1999 年起我国的流行菌型发生了变迁, STX2vha 基因型为主, 占 71.4%; 和国外不同, 羊是主要宿主; 导致 99 年疫情的病原菌至少包括一个克隆群 3 个基因型。

鉴于使用抗生素可刺激志贺毒素基因的表达, 增加发生肾功能衰竭的危险, 筛选到对病原菌有生长抑制作用、没有毒素刺激作用、有预防和治疗作用的嗜酸乳杆菌菌株。发现 EHEC O157:H7 性腹泻病患者, 在出现腹泻病症状的第二天, 18%左右已出现肾功能的损伤的实验室指标, 100%出现出血清 β 2-MG 升高。认为血清 β 2-MG 可以作为早期发现 EHEC O157:H7 患者肾功能损伤指标之一, 提示应在腹泻病阶段就应该注意肾功能的问题。为了提高病原菌分离率, 引进了免疫磁珠分离技术, 发展了免疫胶体金初筛技术, 修改了病原菌分离程序。我国各地分离了许多不产生志贺毒素基因的大肠杆菌 O157, 如何对待这些菌株, 成为 EHEC O157:H7 感染疾病控制工作必须要回答的问题。对 EHEC O157:H7 的 23 个毒力岛的分析结果表明, 这些菌株和 EHEC O157:H7 完全不同, 仅仅携带很少几个可能毒力岛; 鞭毛基因的分析表明, 它们不是 EHEC O157:H7, 而是具有其他多种鞭毛抗原的大肠杆菌 O157。鉴于上述发现, 应该和 EHEC O157:H7 区别对待。有关研究成果, 是我国主管部门制定 EHEC O157:H7 预防和控制措施的主要技术支持和科学依据, 是我国控制 EHEC O157:H7 的主要技术力量, 也为世界控制和预防 EHEC O157:H7, 提供了新的内容和思路。

(荣获 2003 年中华医学科技进步二等奖)

THE STUDIES OF CONTROL STRATEGIES AND EPIDEMIOLOGICAL INVESTIGATIONS OF THE INFECTIONS CAUSED BY ENTEROHEMORRHAGIC *Escherichia coli* O157:H7

Institute of Communicable Diseases Prevention and Control,
Chinese Center for Disease Prevention and Control

The entero-hemorrhagic *Escherichia coli* O157:H7 (EHEC O157:H7) was identified as the causing agent of the mysterious disease outbreak occurred in China in 1999, based on the clinical, epidemiological, serological and bacterial evidences. The studies for understanding the unusual phenomena observed in field have resulted in the new methods, idea, technical procedures and strategies for prevention and control of the infection caused by EHEC O157:H7 in China and on

the world as well.

Because of the unique epidemiological features observed, we assumed that the domestic animals harboring EHEC O157:H7 was the source of infection by shedding the pathogen in feces into environmental; the contaminated food, meat, vegetables and house-fly transmitted pathogen to human; the appropriate personal and house-hold hygiene played critical roles in the outcome.

In an attempt to investigate the source and routes of the infection, strains isolated from China in the period from 1986 to 2002 from various sources were investigated using pulsed-field gel electrophoresis (PFGE). The PFGE analysis is the bases of so-called PulseNet which is a national network of public health and food regulatory laboratories initially established in the US to detect clusters of foodborne disease and respond quickly to foodborne outbreak investigations. The results indicated that the outbreak was caused by same strains with three genotypes, which were isolated from goats, pigs, cattle, hens, as well as from mutton, pork, salted vegetables and flies. The EHEC O157:H7 were also isolated from dung beetles *Catharsius molossus*, captured below ground at Tongshan County, Jiangsu Province of China, where outbreak was observed. Therefore, the dung beetle might acquire pathogenic *E. coli* O157:H7 through contact with feces of domestic animals and has potential to transmitted pathogen to environmental and human by its social activities.

In the 4 years surveillance carried out in provinces of Jiangsu, Anhui and Henan from 1999 to 2002, where clusters of patients with hemolytic uremic syndrome (HUS) were diagnosed, the prevalence of EHEC O157:H7 in cattle, goat, hens and pigs were investigated. It was observed the high prevalence in domestic animals in the three provinces was statistically correlated with number of HUS patients. Our observation indicated that in the rural areas of China, the prevalence of *E. coli* O157:H7 should be monitored to predict possible outbreak or epidemic.

The Shiga toxin 2 (Stx2) subtyping of EHEC O157:H7 isolates revealing that the Stx2vha were the subtypes mostly detected in China (71.4% of the total isolates) since 1999, and three genotypes in signal PFGE group were involved the outbreak of 1999, such as stx2-vha, stx1-stx2 and Stx2. Furthermore, the goat was the first time to be identified as the primary reservoir, followed by cattle, pig and hens respectively.

The supportive treatment for diarrhea caused by EHEC O157:H7 has been recommended. The using of antibiotic is controversial because most antibiotics may cause Shiga toxin-encoding bacteriophage induction and enhanced Shiga toxin (Stx) production, resulting in the higher risk of development of HUS. We isolated a strain of *Lactobacillus acidophilus* LA1, which could inhibit the growth of *E. coli* O157:H7 without enhancing Stx-gene expression in vitro. Using streptomycin-treated mice as model, we demonstrated that oral administration of *L. acidophilus* LA1 dramatically decreased the severity of diarrhea and lowered STEC colonization levels in the gastrointestinal tract and Vero cell cyto-toxicity of fecal samples and. The histological damage to the intestinal mucus induced by *E. coli* O157:H7 were also decreased. This observation indicated that *L. acidophilus* has potential to be developed as the safe and effective anti-bacterial medicine for treatment of infection caused by EHEC O157:H7.

The predictive factor for diarrhea patients caused by EHEC O157:H7 to develop HUS are proposed to include urinal protein and/or occult blood, abrupt increase of white blood cell count, urinal NAG, alpha 1 microglobulin, beta 2 microglobulin, low osmolar urine, high thrombomodulin level and others as well. We observed that the kidney damage could be observed as early as second day of in 30% of bacteriological-confirmed diarrhea patients, such as urine protein. The elevated concentration of serum β 2-microglobulin was observed in all of the diarrhea patients infected by EHEC O157:H7, 31 of 31 patients of hemolytic uremic syndrome (HUS) caused by EHEC O157:H7, 27 of 36 non-O157 diarrhea patients and 4 of 30 age-matched healthy people, with the mean concentration of 3.32 ± 0.81 , 11.27 ± 4.14 , 2.75 ± 0.86 and 1.79 ± 0.29 mg/l respectively. It seems that serum beta 2-microglobulin has potential to be used as one of

predictive parameters for development of HUS in diarrhea patients infected by *E. coli* O157:H7.

The Shige toxin negative *E. coli* O157 has been frequently isolated from various samples in China, which risen the issue of its public health significance. By analyzing the *flhC* gene encoding flagella, it was found that these isolates having various flagella such H11, H12, H16, H19, H38, H42 and un-typeble flagella antigen. We analyzed 22 of the 177 O-islands *E. coli* O157:H7, such as 4 well-characterized pathogenicity islands, 10 putative pathogenicity islands and 8 putative adaptive islands. It was found that all of the Stx-positive *E. coli* O157:H7 isolates have all of the O-islands detected. In contrast, the Stx-negative *E. coli* O157 only has few O-islands. The results suggested that the Stx-negative *E. coli* O157 differ in nature of virulence genes and pathogenicity island.

(Won the Second Prize of Chinese Medical Association for Science and Technology)

我国主粮中伏马菌素污染及串珠镰刀菌分子生物学研究

中国疾病预防控制中心营养与食品安全所 刘秀梅等

串珠镰刀菌 (*Fusarium moniliforme*) 是在全球范围内广泛分布于自然环境中的重要产毒真菌, 主要污染谷物, 并在生长基质中繁殖代谢, 产生多种真菌毒素。伏马菌素 (Fumonisin) 是国际上于 1988 年首次报道的主要由串珠镰刀菌产生的一组新的真菌毒素, 包括 FA、FB、FC 和 FP 等多种组分。其中 FB1 污染最普遍, 毒性也最强。2001 年 FAO/WHO 食品添加剂联合专家咨询委员会 (JECFA) 对伏马菌素可能造成的人或动物的安全性进行了危险性评估, 使其成为真菌毒素领域继黄曲霉毒素之后的又一食品安全关注焦点。

本项目在国家自然科学基金和卫生部科研基金的连续资助下, 进行了八年的系统研究。

伏马菌素污染及串珠镰刀菌生态分布: 首次对我国居民主粮中伏马菌素 B1 (FB1) 污染水平进行调查, 发现我国三大谷物 (玉米、小麦、大米), 特别是玉米中的 FB1 污染严重, 与全球 FB1 的监测结果相符。从谷物及土壤中分离串珠镰刀菌 104 株、串珠交孢变种 24 株, 其中产 FB 菌株 65 株 (10 株 FB1 高产毒株和 7 株 FB3 高产毒株)。为提出我国粮食中 FB 限量标准, 保护人民健康、促进国际贸易提供了基本的科学资料。

串珠镰刀菌及伏马菌素产毒菌株的分子生物学研究: 以真菌 18S、5.8S、28S 及其间区 ITS1、ITS2 DNA 序列为基础, 分别设计了串珠镰刀菌 ITS2 序列 I 型、II 型特异性引物对 Fu5/Fu4、Fu3/Fu2 及镰刀菌属特异的引物对 Fu3/Fu4, 建立了特异的串珠镰刀菌 PCR 检测技术; 以伏马菌素生物合成酶基因为基础, 设计了 3 对引物 P1/P2、P3/P4 和 Fum5F21/Fum5R, 建立了伏马菌素产毒株 PCR 鉴定技术, 32 株分离菌株的 FB 产毒基因测定结果与生物合成毒素的 HPLC 测定结果符合率良好; 运用分子生物学技术分析了来自不同地区菌株的产毒基因多态性及遗传变异性, 对我国不同地域、不同来源的产毒串珠镰刀菌及部分 ATCC 典型菌株进行 rDNA 及其间区序列分析, 并与美国、南非等地的菌株进行序列分析比较, 发现我国产毒基因阳性菌株 rDNA 间区 ITS2 可变区为 I 型特异性, 与南非菌株一致。在串珠镰刀菌及产毒株的分子生态学及亲缘关系等领域有了新的突破, 填补了国内空白, 达到国际先进水平。

伏马菌素检测技术及 FB 抑制人体神经鞘脂类代谢的研究: 率先在我国建立了检测食品中 FB 的 HPLC 方法 (灵敏度为 12 $\mu\text{g}/\text{kg}$); 首次在我国研制了抗 FB1 的单克隆抗体, 建立了 McAb-ELISA 方法, 灵敏度为 10ng/ml, 达到国际水平。在国内率先建立了检测人尿中神经鞘氨醇 (So) 和二氢神经鞘氨醇 (Sa) 的 HPLC 方法, 克服了国外同类方法难以检测男性人尿中低浓度 Sa 的不足, 并在国际上首次报道了人体暴露试验结果, 发现 FB 可以抑制人体

内的神经鞘脂类代谢, 为进一步研究伏马菌素对人类健康的影响提供了技术手段。

本研究发表论文 20 余篇, 英文及与国际会议交流 6 篇, 4 篇被 SCI 收录, 并被国外学者引用。

(荣获 2003 年中华医学科技进步二等奖)

SURVEILLANCE OF FUMONISIN IN STABLE FOOD IN CHINA AND MOLECULAR BIOLOGICAL STUDIES ON *Fusarium moniliforme*

Institute of Nutrition and Food Safety, Chinese Center for Disease Control and Prevention

Fusarium moniliforme is a concerned toxin-producing fungus, which widely exists, in the natural environment, mainly contaminated in grains such as maize, wheat, rice etc. In 1988, Fumonisin were first reported as group of novel mycotoxins, mainly produced by *Fusarium moniliforme*, consisting of FA, FB, FC and FP series etc. FBs are generally occurred in the agricultural products, and FB1 exists extensively and has strongest toxicity. Risk assessments on the potential of fumonisin hazards to the foodstuff safety for human and animals were organized by FAO/WHO Joint Expert Committee of Food Additives (JECFA), which brought out fumonisins being the concerted point on food safety following aflatoxin B1.

Occurrence of fumonisin and ecological distribution of *Fusarium moniliforme*: The first survey on the levels of fumonisin B1 occurrence in Chinese resident's staple grains was carried out. It was found that 3 major cereals including maize, wheat and rice, especially maize, were severely contaminated by FB1. Out of 104 strains of *Fusarium moniliforme* and 24 strains of *Fusarium moniliforme* var. isolated from more than 2000 cereals samples. Ten strains generating high levels of FB1 and 7 strains generating high levels of FB3 were identified from 65 fumonisins-producing strains. The basic information is extremely valuable for bringing forward FB1 tolerance limits in foods, protecting human health and promoting international trades.

Molecular biological Study on *Fusarium moniliforme* and fumonisins-producing strains: Two pairs of type specific primers for *F. moniliforme*, type I and type II, Fu5/4, Fu3/2, and one pair of genus-specific primer for *Fusarium* genus, Fu3/F4 were designed, based on 18S, 5.8S, 28S rDNA and internal transcribed spacer (ITS) sequence of fungi. Three pairs of PCR primers, P1/P2, P3/P4 and Fum5F21/ Fum5R, were designed based on the polyketide synthase gene involved in fumonisins biosynthesis. The specific PCR technique for detecting *F. moniliforme* strains and fumonisin-producing *F. moniliforme* strains were developed. The FB biosynthesis gene was detected from all 32 isolates, which were accordant with the fumonisin determination by HPLC. The rDNA and ITS sequence of the fumonisin-producing *F. moniliforme* isolates in China and 5 typical strains of ATCC were analyzed. It was found that the rDNA highly divergent ITS2 sequences of isolates with positive fumonisin biosynthesis gene from China were type I, which were consistent with a ATCC strain, fumonisin-producing isolates from South African.

Studies on techniques for detecting fumonisin and FB inhibiting human sphingolipid metabolism: Both of the HPLC and McAb-ELISA method for detecting FB in food were first reported in China, the sensitivity were 12 $\mu\text{g}/\text{kg}$ and 10 ng/ml separately. Furthermore, the sensitive HPLC method for determining sphinganine (Sa) and sphingosine (So) in human urine was established in China, which solved the problem that low dilution of Sa in male human urine could not been detected by the similar method in abroad laboratories. The data of human exposure to FBs were first reported in the world and revealed that FB may inhibit human sphingolipid metabolism.

More than 20 papers were published in Chinese, and 6 in English. Four of them had been

collected by SCI.

(Won the Second Prize of Chinese Medical Association for Science and Techology)

我国食物碳水化合物营养学分类及血糖生成指数的基础和应用研究

中国疾病预防控制中心营养与食品安全所、中国医学科学院北京协和医院、
朝阳市第二医院、四川省疾病预防控制中心、北京市第六医院、
宁夏回族自治区疾病预防控制中心、黄石市疾病预防控制中心

本课题利用体外和体内实验等多层面研究,系统地探讨了以食物为基础调节人体血糖、预防和控制糖尿病发生发展的机理和措施。

首次系统地建立了 11 种碳水化合物(CHO)的分析方法,在化学和生理学基础上阐明了膳食纤维(总、可溶性、不可溶性)、淀粉(抗性淀粉、慢消化淀粉、快消化淀粉)的特性和营养学分类;首先提出了不消化碳水化合物和抗性淀粉的概念,突破了以往的基础理论学说,并得到学术界的认可。研究分析了中国 16 个省市常见的 1500 余种食物的 CHO、600 余种食物的膳食纤维和部分食物的抗性淀粉含量,建立了中国食物成分的重要基础数据。通过 1500 多名健康志愿者的试食试验和糖耐量分析,首次完成了我国常见的 160 余种食物的血糖生成指数(GI)数据,填补了国内外空白。通过对中国特有食物和加工方法的研究,阐明了食物品种、物理状况、组成、加工方式与人体血糖生成的关系,阐明了食物中“糖”、“淀粉”有不同的类型,澄清了传统上对“糖”和“淀粉”的错误认识,为我国居民膳食控制血糖提供了科学工具和措施。

首次应用天然稳定同位素 ^{13}C 示踪技术,观察了 60 多名健康人食用不同 CHO 后,在不同时间(4h, 6h, 8h, 12h, 20h, 33h)内的消化吸收过程、血糖应答和吸收利用率。通过不同模型的动物实验证实,含抗性淀粉的低 GI 饲料具有降低餐后血糖和胰岛素应答、提高胰岛素敏感性和血糖向组织转运的比例。抗性淀粉、低聚异麦芽糖、谷物纤维等不消化物在结肠发酵,产生有益菌(如双歧杆菌、乳酸杆菌等)和短链脂肪酸,使肠道内有害产物(如氨、胺和酚类等)的含量和总量降低。抗性淀粉和可溶性膳食纤维对锌吸收利用影响不大。以上结果首次阐明了慢消化和抗性淀粉血糖生成低的发生机理以及对糖、蛋白质代谢的影响。

应用①食物成分数据和血糖生成指数的数据对糖尿病人进行临床营养教育,纠正了“食物交换份法”的误解和错误(如糖是高血糖食品,糖尿病人不能吃水果等)。合理应用食物血糖生成指数的理论,可使糖尿病患者的血糖水平平均下降 15%,减少或停止使用降糖药物人数超过 50%,显著好于其他教育方式,在社会各界引起广泛的应用和好评。②应用食物 GI 数据和淀粉分类学的概念,与企业合作开发了“缓释能量”饼干,该饼干具有吸收缓慢、血糖生成低($\text{GI} < 55$)的特点,首年推出即创产值 16000 多万元。③根据研究结果,推荐我国居民膳食中碳水化合物的每日适宜摄入量为 55~65%总能量、膳食纤维每日适宜摄入量为 30g/d,并于 2000 年已由中国营养学会颁布。膳食纤维的检测方法于 1991 年被定为国家标准,广泛应用于相关领域。

(荣获 2003 年中华医学科技进步二等奖)

STUDIES ON APPLICATION AND FUNDAMENT OF CHINESE FOOD

GLYCEMIC INDEX AND CARBOHYDRATE NUTRITIONAL CLASSIFICATION

National institute for nutrition and food safety, China CDC, et al.

The project was conducted by multi-technologies including both *in vitro* and *in vivo*. The propose of this study is to clarify the mechanism of blood glucose control by diet and the foodstuff classification according to their high or low carbohydrate digested solely, and it's benefits in control the blood glucose of diabetes was studied.

Using chemical test and *in vitro* research, the analytic methods were established for 11 types of carbohydrate, which make it easier to understand the chemical and physiological characteristics of carbohydrate and, by these methods, the contents of carbohydrates in 1500 foods, soluble, insoluble and total dietary fiber and resistant starch contents in more than 600 foods were analyzed. This work provided the basic and unique data in China; according to the digested rate and speed of dietary fiber and starch, a new sub-classification was first suggested as soluble, insoluble and total dietary fiber, resistant slowly digested and rapidly digested starch. Furthermore, 160 common foods were selected and the glycemic index (GI) of these foods were measured by 1500 volunteers. The relationship of food type, physical characteristic, composition and processing with blood glucose response were also studied, the results showed that different types of 'starch' and 'sugar' can have different blood glucose response and GI value. All these works provides useful evidence for people to prepare their foods scientifically and prevent from suffering diabetes and other chronic diseases.

The mechanism of how can carbohydrates control body blood glucose level was studied by using the isotope tract technology of natural stable ^{13}C . More than 60 healthy volunteers were provided with different types of carbohydrates during different test time, and the metabolized process and blood glucose response during 4, 6, 8, 22, and 33hr were observed. The results showed that resistant starch are characterized by slower digested, lower blood glucose response and energy factor (Atwater factor < 4) as well as lower GI value. The results of animal experiment proved that undigested carbohydrate made many health effect such as decreasing the postprandial glucose and insulin response, increasing the sensitive of tissue to insulin and help to maintain a stable blood glucose level, after they reached colon and fermented there, they can stimulate the growth of probiotics (bifid bacteria and lactic bacteria), and increase the production of short-chain fatty acid as well as decrease the harmful matters (ammonia, amine and hydroxybenzene). These can all do good to human being. All these results can help to understand the mechanism and health effect of undigested starch.

The main application of these results:

1) The databases of 1500 foodstuff on carbohydrate, dietary fiber content and GI value in 160 foods have been used in clinical education, and to rectify the traditional incorrect conception. It proved to be a new and effective method of diet guide, some result showed the blood glucose level was decreased by 15% and about 50% of people can decrease drugs by this way.

2) A "Energy Delivered Progressively" biscuit (GI<55) was produced by added slowly digested starch and resistant starch, which obtained a production value of 160 million Yuan RMB in the first year and widely welcomed by diabetics and other people.

3) The adequate intake (AI) of carbohydrate and dietary fiber were suggested by these studies , and promulgated by the Nutritional Society of China in 2000. Now, it is widely used as standard in nutrition filed. The methods of dietary fiber act as a national analytic standard method since 1991 and widely used in the evaluation of food.

(Won the Second Prize of Chinese Medical Association for Science and Technology)

食物残留物的检测技术研究

中国疾病预防控制中心营养与食品安全所

食品安全问题已得到政府与社会的广泛关注，而食品安全检验技术的严重滞后，制约我国食品安全保障体系的发展，引起国家领导和有关部门的高度重视，为加强食品安全卫生，保障与促进我国入世后食品安全健康发展，提高我国食品安全检测技术水平，科技部在广泛征求专家意见的基础上，把本项目列为科技部社会公益研究专项资金资助课题，研究周期为2001年1月—2002年12月，资助金额160万人民币。

本项目涉及金属污染物、农药兽药残留、致病微生物、生物毒素等食品安全领域的多个方面，研究内容主要包括（1）快速检测方法、多残留测定方法；（2）现代生物技术测定方法研究（3）食品耐药性检测技术方法研究，建立耐药性抗菌谱和发展模型；（4）分析方法评价技术研究（5）监测与分析研究，利用已建立的检验方法，进行霉菌毒素、河豚毒素、食源性致病菌耐药性监测（6）“掺假掺伪”测定方法研究。本研究建立了30多个检验方法，包括农药残留快速检验方法及多残留分析方法，15个ELISA分析方法及4个GC-MS方法等现代高新技术技术分析方法；3个“掺假掺伪”测定方法；评价4种国家标准分析方法；首次在国内建立3种致病菌抗菌谱，发展耐药模型；在我国海域内进行河豚鱼毒素测定及可食品种筛选，为开发我国河豚鱼项目提供科学依据。到目前为止，已提交全国食品卫生标准化技术委员会审议通过22个测定方法，其中3个方法已为国标，发表论文15篇。

课题成果的意义：（1）完善了我国食品安全所急需监督检测技术，填补多项国内技术空白，所建立的方法与国际先进方法接轨，提升了我国食品检测技术科技水平，部分成果已上升为国家标准和卫生部政策管理技术文件；（2）提高相应的技术指标或检验参数，以应对国际形势的变换；（3）形成具有我国自主知识产权的物化检测手段，以便大面积推广使用；（4）上述各个方面是改变目前我国层出不穷的食品安全问题的基础保证；（5）多项研究成果已在食品安全监督检测中广泛应用，2001-2002年全国整顿和规范市场经济秩序，食品安全专项整治等活动中卫生部已发文将本研究的成果作为技术规范广泛应用于食品安全监督检测工作中，特别是“吊白块”、“瘦肉精”测定方法，在全国食品“打假”活动中，起到了技术保障作用，有效抑制了“吊白块”、“瘦肉精”在食品中的滥用，为现阶段食品安全保障做出贡献。

（荣获2003年中华医学科技进步三等奖）

STUDIES ON THE DETERMINATION METHODS OF RESIDUA IN FOODS

National institute for nutrition and food safety, China CDC

There is mounting concern about food safety at the national and regional levels countrywide in China. In the past few years, inadequate capacities in determination of contaminations in foods were a major obstacle in the development of all strategies related to food safety. In order to provide safe, high-quality foods that meet the consumer's demands, improve the development of our food safety system, and strength the capacities in determination of contaminations in foods especially China joining the WTO, a project about the detection of residua in foods, financially supported 1.60 million RMB by the Ministry of Science and Technology, P.R.C was conducted between 2001 and 2002. Heavy metal, pesticide residues, veterinary drug residues, foodborne pathogens, biotoxins and so on were included in this project. Details are as follows.

- (1) Development and validation of rapid methods for the determination of Multi-residues in foods;
- (2) Development of modern biotechnological methods;
- (3) Development of methods for the determination of pathogens antibiotic resistant and establishment of antibiotic resistance patterns and models;
- (4) Evaluation of analytical methods for contaminations in foods;
- (5) Monitoring and analysis of foodborne contaminations (i.e. mycotoxins, tetrodotoxins and pathogens) antibiotic resistant;
- (6) Studies on the detection of foods adulterated with some illegal additives.

More than 30 analytical methods (ELISA, GC-MS, HPLC and so forth) for the determination of contaminations in foods as well as foods adulterated with some illegal additives were established. Three foodborne pathogen antibiotic resistance patterns and models were established in our country. On the other hand, the detection of tetrodotoxin and the screening of edible puffer fish provide the scientific data for the availability of puffer fish. Twenty-two analytical methods were put forward to the national food hygiene standard association and three of them have been issued as the national standard so far. Fifteen papers related to this project have been published.

Significance of the project:

Some of methods for detection of the residua mentioned above weren't publicly reported so far. All methods obtained in this project will improve the analytical capacities and their application in foodborne contaminants surveillance in China, Some of them have been issued by the Ministry of Health as the national standards and regulations. This project has improved the technological indexes and parameters in food contaminant surveillance. The rights of all analytical methods developed have reserved in China. The results obtained in this study will provide an effective platform for reducing the foodborne diseases and make the food safer in China. Besides, most of the analytical methods have been applied in food safety control and inspection and created a significant effect to the development of economy and science in China.

(Won the Third Prize of Chinese Medical Association for Science and Techology)

呼吸道吸入天然钍 (Tho2) 和稀土矿尘联合作用的研究

中国疾病预防控制中心辐射防护与核安全医学所

陈兴安 高凤鸣 王玉珍 肖慧娟 程永娥 陈 莲 杨英杰 甄 荣 韩轩茂

本项目属于放射卫生学。包头白云鄂博稀土铁矿是世界最大的稀土资源，已开采 40 余年，研究该矿在开采中产生含钍稀土矿尘对矿工健康的影响，是保护矿工健康和采取防护措施的科学依据。

本课题先后得到了国家自然科学基金委和国际原子能机构的资助，自 1987 年起到 2002 年，中间用了 8 年时间，采用多学科，多层次的协同研究，通过现场人群调查与动物实验，其中包括流行病学调查、矿工职业查体、人体肺内钍活度的测定，以及钍尘对大鼠的诱癌实验，钍在大鼠体内的排泄规律，大鼠肺部所受剂量的估算、离体细胞培养试验、DNA 修复实验等，进行综合分析，取得了重大突破。

在研究手段上，在国内首先应用了性能为国际先进水平的高灵敏度呼出气中钍射气 (Rn-220) 活度测定装置，可直接推算出矿工肺内钍尘的沉积量，结合 X 线胸大片所见，在国内外首先发现在活体条件下当工人肺内含钍稀土矿尘量达到约 755mg 时，将引起 0+期尘肺，为防止尘肺的发生提供了新的监测手段。

本研究中最重要突破时在国内外首先用人群资料证明长期吸入含钍稀土矿尘可致肺

癌。在对白云鄂博矿 3016 名接尘矿工进行肺癌死亡率的后回顾性调查中, 接尘组与对照组对比, 同期(1994 年 1 月至 2001 年 3 月间)接尘组增加了 10 例肺癌死亡病例(经调查分析同吸烟无关), 而对照组无一例, 两组 SMR 差别十分显著。这种主要由于长期吸入较高浓度的含钍稀土矿尘(致癌源为二氧化钍和二氧化硅)和次要因素即工作场所空气中较高浓度的钍射气短寿命子体所诱发的肺癌, 平均诱发期为 38.5 年。此发现结束了国内外长期认为上述矿尘只能引起混合尘肺的普遍看法, 是学术上的历史重大突破, 具有重要的科学意义和社会效益。

(荣获 2003 年北京市科技进步二等奖)

禽 H9N2 亚型流感病毒感染人的发现及其意义

中国疾病预防控制中心病毒病预防控制所

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首先从血清学调查入手, 发现我国南北方人群中均测出 H9 毒株的抗体。在病原监测中, 于 1998 年和 1999 年先后两次从流感样患者中分离到 6 株 H9N2 毒株。为了解分离物来源及排除实验室污染的可能, 进行了个案调查和病毒株抗原性和基因特性分析。结果表明, 分离物均属禽 H9N2 亚型毒株, 其可能性最大来源于鸡的 H9N2 毒株, 实验室污染可能性可完全加以排除。同时发现 A/广州/333/99 (H9N2) 病毒与 H9N2 病毒 G9 和 G1 基因系毒株的基因重配子, 它的 PB2, PB1, PA 和 M 基因节段来自 G1 毒株基因系, 而 HA, NA, NP 和 NS 基因节段来自 G9 毒株基因系, 而且还发现我国内地禽中至少同时流行着两系(G9 和 G1)抗原性和基因特性不同的 H9N2 毒株。除此以外, 还发现了对鸡具有高致病性的 H9N2 毒株, 同时提出了鸡在流感大流行株起源中作用不亚于鸭的见解。

禽 H9N2 毒株能感染人, 并能在自然界中发生基因重配, 同时重配子能感染人均在国际上首次发现, 此发现表明禽流感病毒能直接感染人, 也可能原先对人不致病的禽流感病毒, 通过基因重配形成了对人致病重配子。因此上述发现彻底揭开流感大流行株起源及我国流感多发的原因提供了新的科学依据, 证实了禽流感一种新出现的传染病, 为国际反生物恐怖及流感大流行防治策略制定提供了新内容。

对鸡具有高致病性 H9N2 毒株发现及弄清内地禽中 H9N2 毒株基因类型对流感监测、诊断及防治方面均具有重要意义。

因此, 上述发现不仅在理论上, 而且在实际上均具有重要意义, 并具有显著的社会和经济效益。

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