

《关于禁止发展、生产和储存细菌(生物)
及毒素武器和销毁此种武器的公约》
缔约国会议

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议程项目 6

常设议程项目：

审查与《公约》有关的科学技术领域的发展

生物技术发展及其对《禁止生物武器公约》的影响¹

中国代表团提交

1. 近年来，生物技术发展迅速，合成生物学、基因组学、系统生物学以及使能技术等领域的的发展尤为引人注目。这些发展一方面极大地促进了生命科学的进步，对揭示相关疾病的致病机理和制定有效防治措施具有重要意义；另一方面其负面效应也日益凸显，产生了新的风险与挑战。

一、 合成生物学

2. 合成生物学研究取得了巨大发展，从单一基因到完整代谢通路、整条染色体的合成，并形成具有完全生命特质的微生物已成为现实。由于它对人类生命健康、社会经济及环境等的潜在贡献及其可能谬用所产生的安全风险，合成生物学的发展受到极大关注。目前利用合成生物学手段，已经成功构建、合成大量标准 DNA 调控元件或“模块”，利用这些标准元件进一步构建可以实现特定功能的完整遗传调控网络或通路。利用合成生物学技术，在酵母中实现萜类化合物生物合成，用以生产抗疟药物前体青蒿酸，即是利用合成生物学技术发展新型抗微生物药物、促进人类生命健康的一个典型例子。2010 年完整细菌基因组的合成、其在已经去除基因组的“空壳”细胞中的成功复制并导致全新细菌类型的出现，是合成生物学发展的重大事件。

¹ An English unofficial translation is included after the Chinese text,

3. 近年来作为合成生物学支撑的高通量 DNA 合成技术的迅速发展，进一步降低了合成生物学的技术“门槛”，使 DNA 合成变得更加快捷、便宜和高效，其被滥用的风险也越来越大。

4. 自动化的 DNA 高通量合成与组装，一方面大大提高了不同国家获得相关研究材料的机率，同时也为有效监控提供了一定可能。可以通过建立与病原微生物 DNA 数据库相联的合成订单筛选系统，对不同客户提供的订单进行后台分级管理，对那些与病原微生物 DNA 相关的合成及其后续工作，实现全过程有效监控。

二、 基因组学

5. 自从 2003 年完成首个人类基因组全测序以来，基因组学发展迅速，各种大规模基因组测序计划如千人基因组计划、地球微生物组计划（the Earth Microbiome Project）等也相继开展。千人基因组计划等相关研究迅速发展，使大量人群特异性遗传变异及其生物学功能得到确定，而人类特异性遗传变异与某些传染性疾病易感性之间的关系也相继得到证实。这为利用合成生物学、反向遗传学、基因组体外定向进化等手段，对整个病原微生物进行基因组的定向改造，提高致病性、传染性、宿主特异性等提供了理论和现实可行性。最近人为改造高致病性 H5N1 禽流感病毒传染性和宿主特异性获得成功，提示相关研究被滥用的现实可能性大大提高。

6. 此外，在高通量测序技术的推动下，人体微生物组学也取得了重要成果，发现不同人群可能存在与饮食等外在环境、自身遗传等密切相关的人群特异性微生物组，即人体第二基因组，而且这些人群特异性微生物组与人体正常生理功能密切相关。人体正常微生物组的紊乱，必将影响人体正常生理代谢并导致疾病的出现。这为通过饮食、特定微生物等隐秘手段进行人群特异性攻击提供了另外一种可能。而纳米材料、纳米技术的进步，更为人为设计改造相关微生物的有效投放与递送提供了重要工具和手段。

三、 系统生物学

7. 基因组、转录组、蛋白质组、代谢组等组学研究迅速发展，系统生物学应运而生。系统生物学寻求整合上述多层次的生物知识，建立用于描述、并最终可预测的数学模型来综合实验知识与计算工具，以便研究构成生物系统各组之间的相互作用。然而由于生物系统的复杂性，在可预见的未来数年内，要实现上述目标依然十分困难。

四、 使能技术研究

8. 使能技术(enabling technologies)是生命科学研究高速发展的支撑和基础。通信技术的发展将有利于计算及数据资源，以及研究与应用能力的全球扩散，促

进生命科学发展更快更便宜。互联网，以及电子信息与移动通信的迅速发展将进一步促进全球科研合作以及科学信息的播散。

高通量系统

9. 高通量系统通过样本的平行分析极大地提高了分析的速度与能力，作为研究工具支撑着许多领域，如基因组学、蛋白质组学、系统生物学以及合成生物学等的活跃研究。高通量质谱技术日益强大并被广泛运用，如用于分析生物样本中的蛋白和多肽，并支撑着蛋白质组学研究。这些技术使得快速及灵敏确认微生物及毒素成为现实，质谱技术同样能用于微生物核酸的高通量分析，这对于非可培养的微生物检测极为有用。这些技术的发展将有利于与《禁止生物武器公约》相关的监测、诊断和生物法医学。

DNA 测序

10. DNA 测序技术是发展最快的领域之一，第二代 DNA 测序系统每天可完成读长为 100bp 的 250 亿碱基的读取。随着 DNA 序列分析速度的快速提升，其测序成本快速下降。随着第三代测序系统的出现，1000 美元完成一个人基因组的测序目标指日可待。

11. 高通量测序技术的迅速发展，有利于病原微生物基因组、宏基因组等的迅速测定，为其基因组的演变及其与传染性、致病性的关系等研究提供便利，将极大促进相关疫情的监控、诊断和治疗。但是这些 DNA 序列数据也可能被用于人工合成新型病原体，以及改造病原体的抗原性、感染特异性、毒性以及抗药性，使传统的传染病应对手段失效，导致传染病的预防控制难上加难。

计算机技术

12. 不断增强的独立超级计算机系统已经建立，包括用于生命科学中研究计算密集问题的专用计算机。比如，可用于分子动力学模拟来研究蛋白与核酸的折叠和相互作用、药物与受体的相互作用等。而另一种获得超级计算能力的方法是分布式计算，这种技术是通过联网的个人计算机，来获得与超级计算机相等的计算能力。较为成功的分布式计算的例子是 Folding@Home，从 2000 年 10 月 1 日起，全世界有超过 500 万 CPU 参与 Folding@Home 计划，使其与全世界最大的计算机的能力相当。

The Effect/Impact of Biotechnology Progress on BWC

Submitted by China

1. During the recent years, biotechnology has made great advances. The development in some areas, such as synthetic biology, genomics, systematic biology and enabling technologies, is especially noticeable. On one hand, these developments have greatly promoted the improvement of biological sciences, which is of great importance for the elucidation of molecular mechanisms of relevant diseases and design of efficient prevention and treatment measures. On the other hand, these developments have created new challenges and risks, and the negative effects have become more obvious.

I. Synthetic biology

2. From the synthesis of a single gene, single pathway, single chromosome to the totally chemical synthesis of the whole microbiological genome with life features, synthetic biology has made remarkable progress. Due to its impact on human health, social and economic development, and even the environment, as well as its potential risks of misuse, the development of synthetic biology is attracting much attention. At present, the diverse standard DNA regulatory elements or modules have been designed, synthesized and deposited, which can be further combined to construct whole pathways, complex genetic networks with special functions. The artificial design and reconstruction of terpenoid synthesis pathways and biological production of Artesunate acid, the precursor of antimalarial drug in yeast are cases of typical successful application of synthetic biology to the green production of medical drugs to facilitate the human health. Creation of a new form of bacterial cell controlled by a totally chemically synthesized genome which was transferred to a genome DNA repelled “empty cell” is a great event during synthetic biology development.

3. The rapid advancement of high-throughput DNA synthesis has greatly reduced the technical “bottle neck” of synthetic biology. As DNA synthesis becomes faster, cheaper and more efficient, the risks of its misuse are greatly increased.

4. The high throughput/automatic DNA chemical synthesis and assembly have greatly facilitated the availability of research materials of different countries, while providing a good opportunity for the efficient monitoring and control of DNA synthesis. By establishing commercial order sorting, filtering and differential authorizing website administration system connected to the central pathogenic

microbiology genome database, the whole process of researches related to pathogenic microbes can be efficiently monitored and controlled.

II. Genomics

5. Ever since the Human Genome Project was completed in 2003, relevant researches are developing rapidly. Different large-scale genome projects, such as 1000 Genomes Projects, the Earth Microbiome Project, are under way. While the results of 1000 Genomes Project and other relevant researches have revealed diverse human population specific genetic variations and associated functions, the GWAS (Genome-wide association study) has strongly indicated that the population-specific genetic variation is related to disease sensitivity. The confirmation of the correlation between genetic variation and disease sensitivity makes it possible to improve the specific microbes' pathogenicity, infectivity, and host specificity using combinatorial approaches of synthetic biology, reverse genetics and whole genome in vitro directed evolution. Recently, the successful change of the infectivity and host specificity of high pathogenic H5N1 avian influenza suggests that the potential and practical risks of misuse of relevant researches are increasing.

6. Thanks to the rapid progress of high-throughput next generation sequencing, the human microbiome research has revealed that our human body is closely associated with specific microbiome or human second genome that might be highly correlated with human genetics and exogenous environment elements such as dieting. The primary results of human microbiome researches also indicate that our normal physiological functions are closely related to our second genome, whose disorder might affect normal physiological metabolism of humans and even cause illness. The strong correlation of our second genome with our physiological functions provides an alternative cryptic approach to attack human population specifically through population specific microbes, even daily dieting. The rapid development of nanomaterials and nanotechnology will also provide important tools for and approaches to efficient delivery of artificially modified and designed microbes.

III. Systematic biology

7. In recent years, the "x-omics" such as genomics, transcriptomics, proteomics and metabolomics have undergone great development. Systematic biology was born at the right moment. By integrating biological knowledge/information at different levels, systematic biology seeks to develop a describable, predictable mathematical model to synthesize experimental data and computational tools. The ultimate goal of systematic biology is to use the model to study the interactions of individual biological compartments. Because of the extremely large scale and complexity of "x-omics"

datasets, it is still quite difficult to establish a reasonable mathematic model in the near and foreseeable future.

IV. Enabling Technologies

8. Enabling technologies are the cornerstones of rapid progress of biological study. Communication technology will facilitate the global distribution of computing and data resources, and the capacity of fundamental research and development, promoting more rapid and cost-effective development of biological studies. The rapid development and integration of the internet, electronic & information engineering and mobile communication will further boost global collaboration in scientific research and spread of scientific information/knowledge.

High throughput system

9. The high-throughput system has greatly increased the speed and capacity of functional analysis via parallel sample preparation, treatment and detection. As an emerging and highly efficient research tool and support system, high-throughput technology is extensively used in many active areas, such as genomics, proteomics, systematic biology, synthetic biology. As the cornerstone of proteomics, the increasingly robust high-throughput mass spectrometry technology is widely used to quantitatively analyze protein and peptide samples, which makes it possible to detect and confirm microbes and toxins rapidly and sensitively. Mass spectrometry (MS) can also be used for high-throughput nucleic acids analysis, which is particularly useful for the detection of uncultivable microbes. Hence, the development of high-throughput MS technologies will facilitate the surveillance and diagnosis of BWC relevant agents, and forensic medicine.

DNA sequencing

10. DNA sequencing is one of the fastest-developing fields. The second generation sequencing system can reportedly read up to 25 billion bases of DNA per day in 100 base pair read lengths. With the rapid increase in DNA sequencing capacity, the costs of DNA sequencing will be greatly reduced. With the more robust third generation sequencer on the horizon, the cost of sequencing an entire human genome is likely to be below \$1000.

11. The rapid development of increasingly efficient high-throughput sequencing technologies is essential for the rapid sequence determination of the pathogenic microbes' genome and environmental metagenome, which will definitely facilitate the revelation of pathogenic microbes' genome evolution and its relation with infectivity and pathogenicity and greatly enhance the surveillance, diagnosis and therapy of

related infectious diseases. There is no doubt that such DNA sequence information can also be used for the modification of antigenicity, infectivity, toxicity and drug resistance of traditional pathogens, even for the artificial design and synthesis of totally new pathogens, which will lead to the failure of traditional prevention and treatment of infectious diseases and make efficient prevention and control more difficult.

Computing technologies

12. The increasingly robust multithread supercomputers have been assembled worldwide. Some have been specially assembled for data-intensive computing in biology, such as molecule dynamic simulating to study folding and interactions of proteins and nucleic acids, the interactions of drugs and receptors. Another means to obtain supercomputing capacity is the distributed computing system which incorporates hundreds of thousands of internet-connected PCs throughout the world to achieve the comparative capacity of supercomputers. One successful example is folding@Home project which combines more than five million CPUs since October 1, 2000 to obtain the capacity of the most powerful supercomputers.
