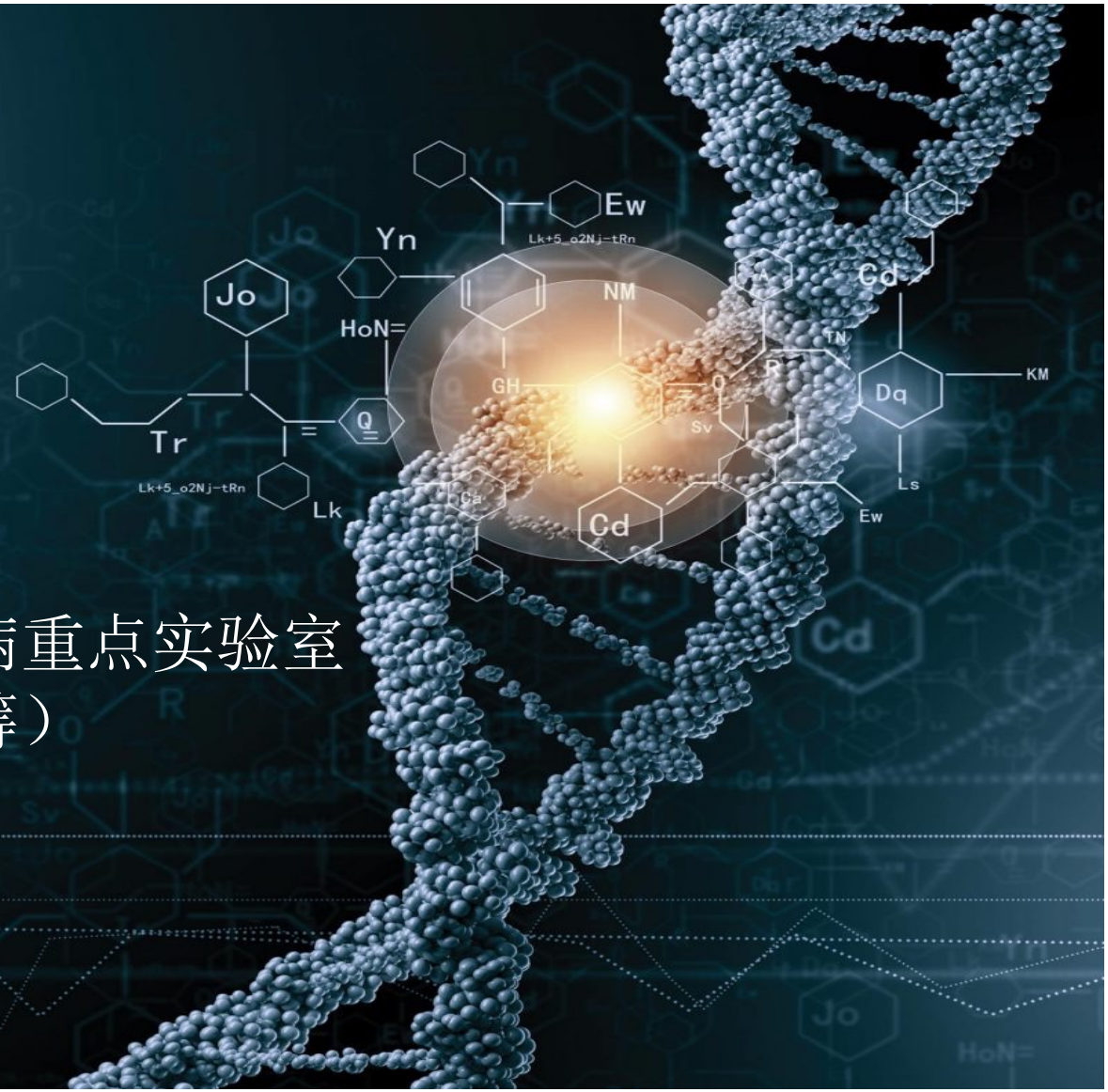
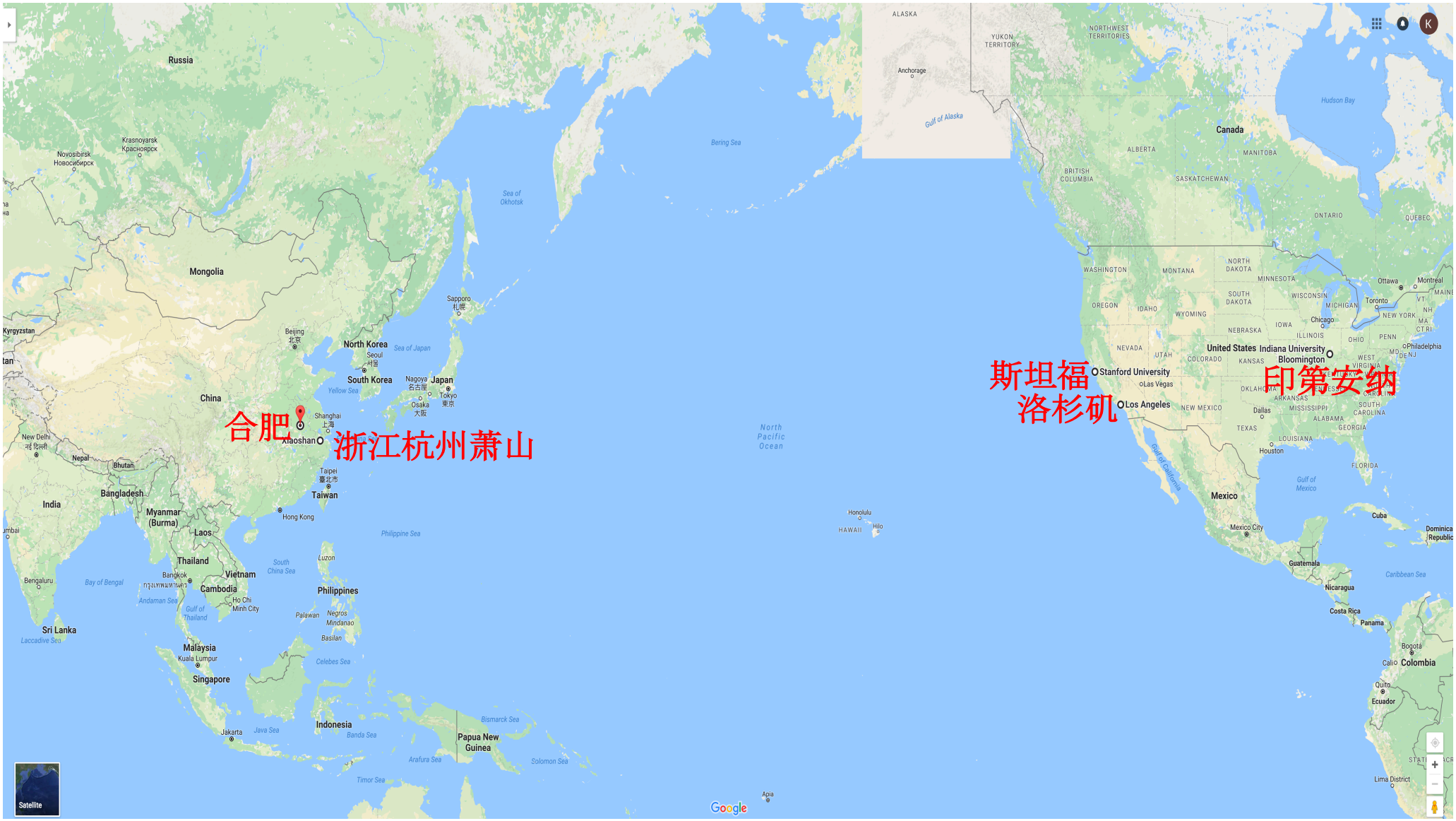
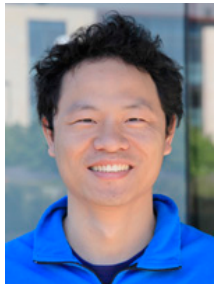
生物大数据和精准医疗
--少年班宣讲

瞿昆，教授，青年千人
生命科学学院、医学中心、
中科院天然免疫和慢性疾病重点实验室
合肥微尺度国家实验室（筹）
中国科学技术大学




合肥
浙江杭州萧山
斯坦福
洛杉矶
印第安纳
Russia
Mongolia
China
North Korea
South Korea
Japan
Taiwan
India
Canada
United States
Mexico
Stanford University
Los Angeles
Indiana University Bloomington
Bering Sea
North Pacific Ocean
Philippine Sea
Sea of Okhotsk
Sea of Japan
Yellow Sea
Hudson Bay
Gulf of Alaska
Gulf of California
Gulf of Mexico
Caribbean Sea
Bay of Bengal
Andaman Sea
Gulf of Thailand
South China Sea
Celebes Sea
Bismarck Sea
Arafura Sea
Timor Sea
Java Sea
Banda Sea
Solomon Sea
Laccadive Sea
Satellite
Google

师者，所以传道、授业、解惑也



选择比努力重要一万倍

努力比天赋重要一万倍

In Treatment for Leukemia, Glimpses of the Future　　2012年7月7号,《纽约时报》

Biosketch

EDUCATION

1995-1998	BS with Honors in Molecular Biology, University of Wisconsin, Madison, WI
1999-2005	MD, Washington University School of Medicine, St. Louis, MO

POST-GRADUATE TRAINING

2004-2005	Research Assistant (laboratory of Dr. Stuart Kornfeld), Division of Hematology, Washington University School of Medicine
2005-2007	Internal Medicine Resident, Barnes-Jewish Hospital/Washington University School of Medicine
2007-2008	Clinical Hematology/Oncology Fellow, Barnes-Jewish Hospital/Washington University School of Medicine
2008-2011	Research Hematology/Oncology Fellow (laboratory of Dr. Timothy Ley), Stem Cell Biology Section, Washington University School of Medicine

ACADEMIC POSITIONS & EMPLOYMENT

2008-2011	Bone Marrow Transplant Gold Physician, Barnes-Jewish Hospital
2011-2013	Instructor, Division of Oncology, Department of Medicine, Washington University School of Medicine
2013-present	Assistant Professor, Division of Oncology, Department of Medicine, Washington University School of Medicine
2013-present	Assistant Director, Cancer Genomics, McDonnell Genome Institute at Washington University

BOARD CERTIFICATION

2012	Internal Medicine
2014	Medical Oncology

HONORS & AWARDS

1999-2003	Albert F. Koetter, MD Distinguished Student Scholarship
2002	Alpha Omega Alpha
2002	McGraw-Hill and Appleton and Lange Medical Publications Student Award
2002	Lee B. & Virginia G. Harrison Memorial Scholar
2003	The Park J. White Prize in Medical Ethics
2009	Knowlton Award for Clinical Excellence
2010	Fellows' Award from Mayo Clinic Hematology/Oncology Review
2010-2012	National Institutes of Health Loan Repayment Program Award

PROFESSIONAL SOCIETIES & ORGANIZATIONS

2007-present	American Society of Hematology
2007-present	American Society of Clinical Oncology
2016-present	American Society of Blood and Marrow Transplantation

Dr. Lukas Wartman

名牌大学教授、医生

03年诊断患有白血病

久治不愈

基因测序 DNA/RNA

基因FLT3异常表达

肾癌药物靶向FLT3

症状明显缓解

个性化医疗完美案例

http://www.nytimes.com/2012/07/08/health/in-gene-sequencing-treatment-for-leukemia-glimpses-of-the-future.html?_r=2&partner=rss&emc=rss

精准医疗的定义？

"Delivering the right treatment at the right time, every time, to the right person." – Barack.Obama

"每一次，都在正确的时间，给予正确的患者，以正确的治疗方法" – 布莱克.奥巴马

	传统医疗		精准医疗
人	治疗疾病	<---->	治疗病人
物	根据经验	<---->	大数据支持
时	发病后治疗	<---->	实时监控

可以实现吗？

如何实现？

物种间的差异主要源自遗传物质-染色体、DNA

高通量测序

生物信息分析

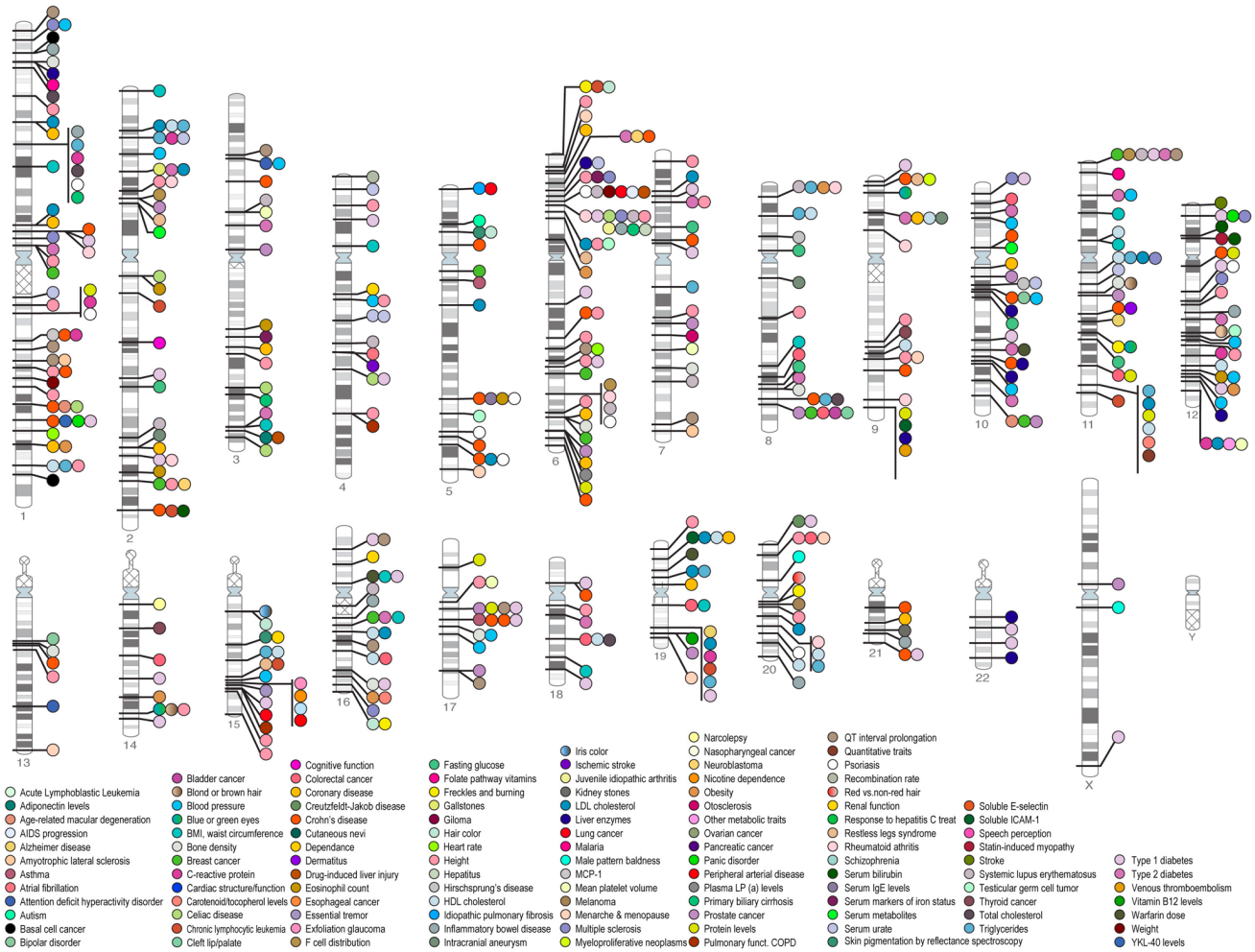
疾病相关DNA变异位点

Sanger sequencing video

Public project sequencing video

Private project sequencing video

全基因组关联性分析（GWAS）



统计数字-截止目前

3990 关联性分析研究

共发现 2,974,967 SNP

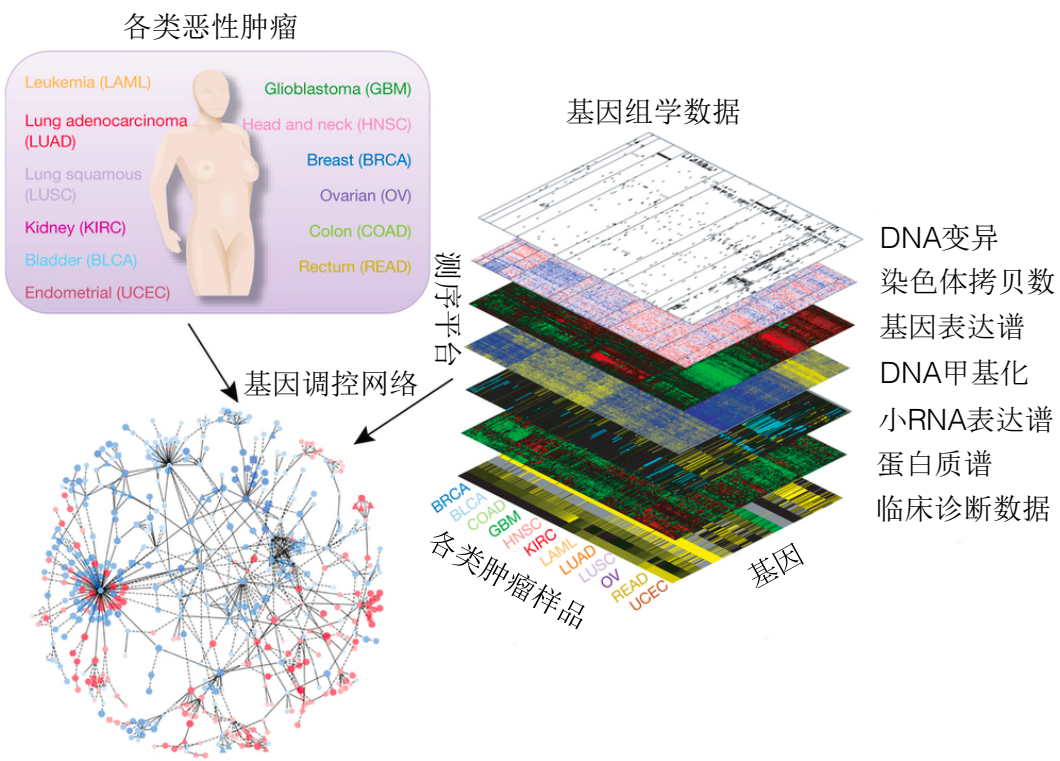
和1991种疾病显著关联

涉及15个以上国家

36个以上种族的

18,679,155人口

癌症基因组计划（美国国家健康研究所）



通过基因测序预测患病概率成为可能

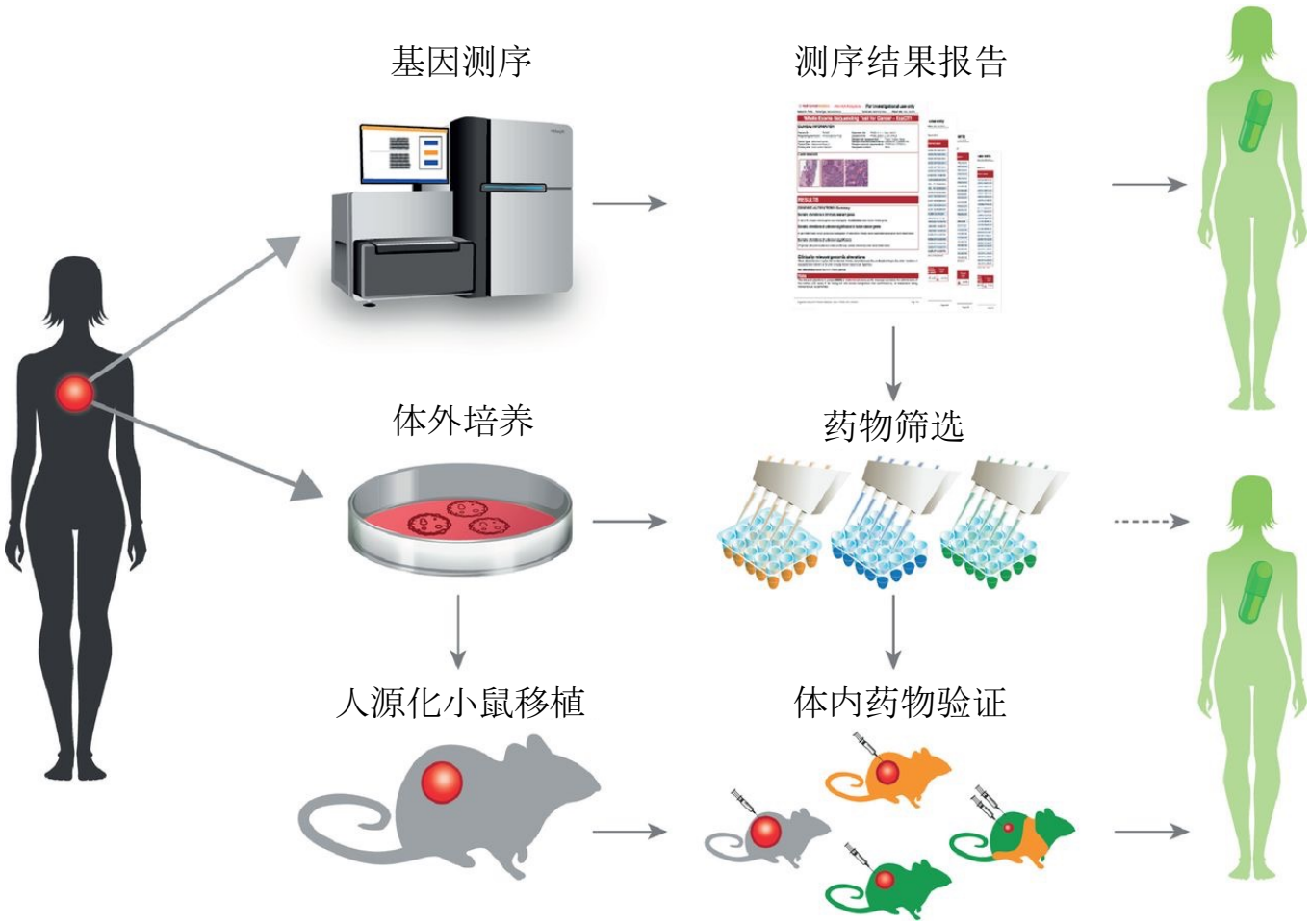
2005年12月	启动
2006年11月	资助测序中心
2007年7月	资助技术发展
2008年9月	第一批数据，恶性胶质瘤
2009年9月	资助数据分析中心
2010年4月	资助大脑研究中心
2010年12月	该计划首批数据上线
2011年7月	卵巢癌基因组完成
2012年7月	结肠癌基因组完成
2013年5月	子宫内膜癌基因组完成
2013年5月	白血病靶向药物筛选完成
2013年10月	恶性胶质瘤基因组完成
2014年1月	膀胱癌基因组完成
2014年7月	肺癌、胃癌基因组完成
2014年8月	肾癌基因组完成
2014年10月	甲状腺癌基因组完成
2015年1月	头颈癌基因组完成
2015年6月	皮肤黑色素瘤基因组完成
2015年10月	小叶性癌基因组完成
2015年11月	肾细胞癌基因组完成
2015年11月	前列腺癌基因组完成

……

……

原始数据共享

精准医疗1.0



原发性
非小细胞肺癌

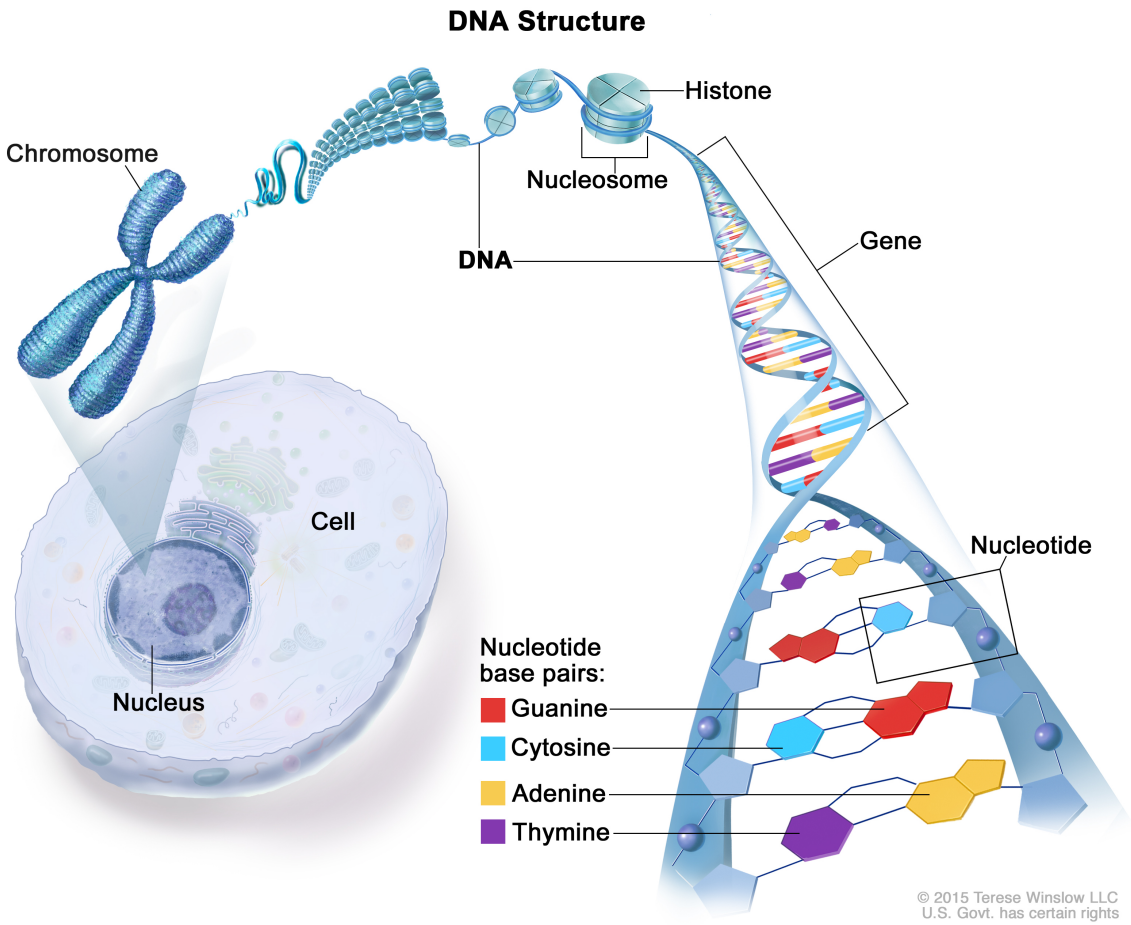
EML4-ALK 突变
↓
克里唑蒂尼

EGFR 突变
↓
易瑞沙/特罗凯

K-RAS 突变
↓
传统的放化疗

DNA测序仅仅只是一个开始

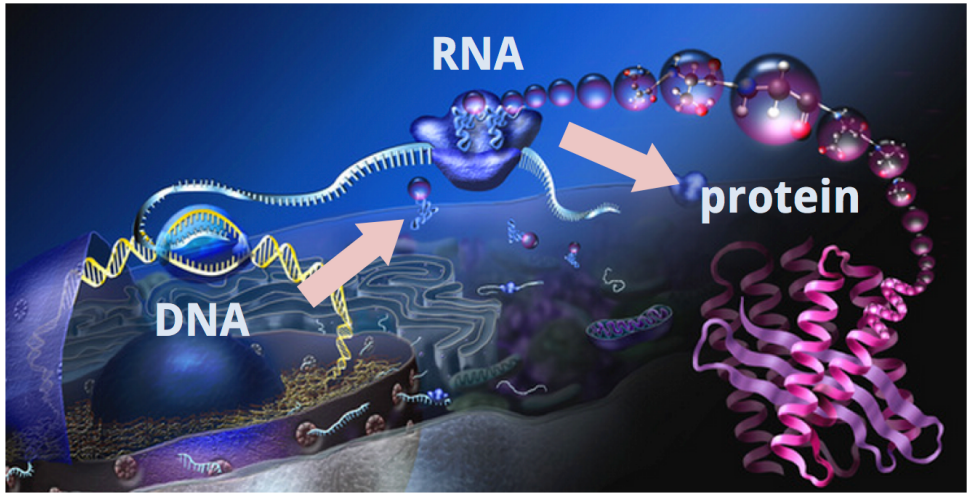
DNA序列并不能决定一切 → 基因表达的表观遗传调控



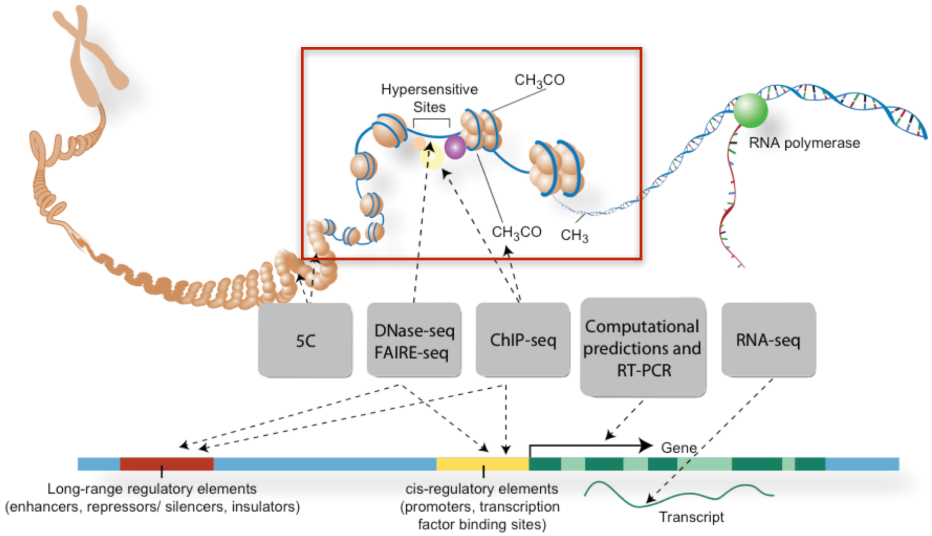
现代生物学最重要的基本规律

中心法则

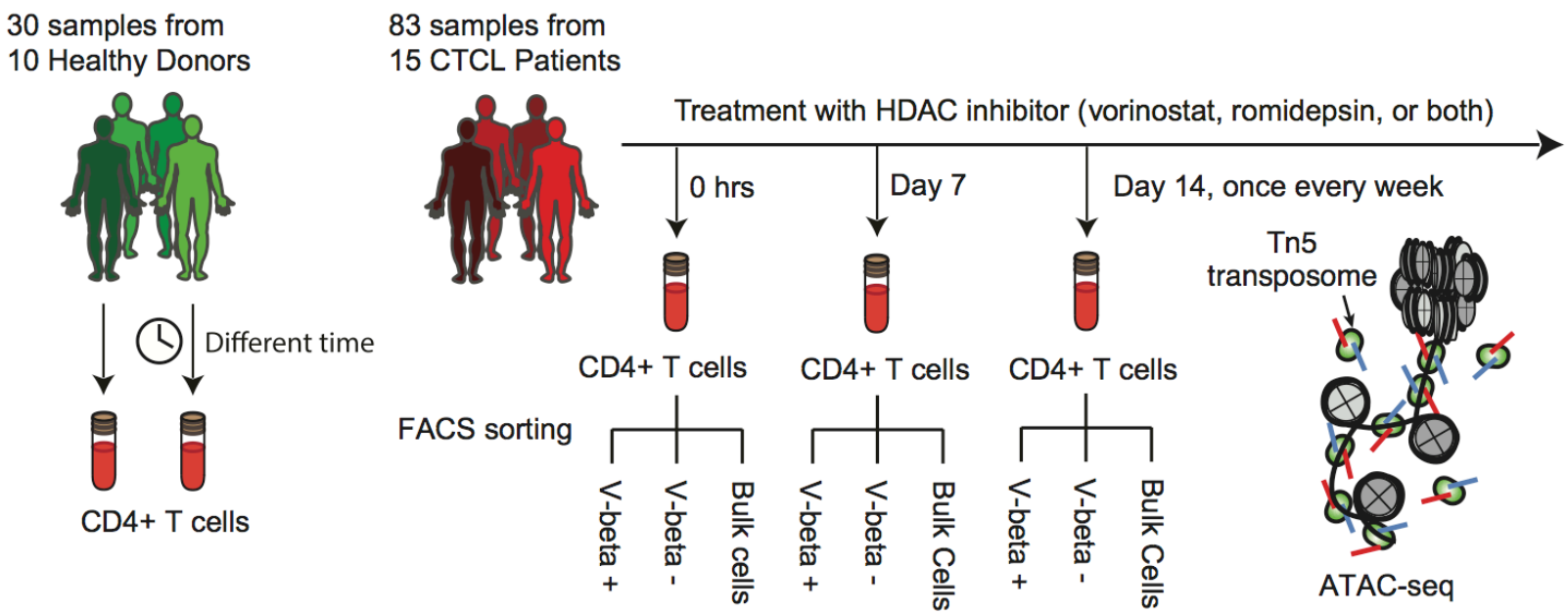
DNA序列只是其中的一部分
对遗传信息传递的调控机制
决定着另外的很大一部分

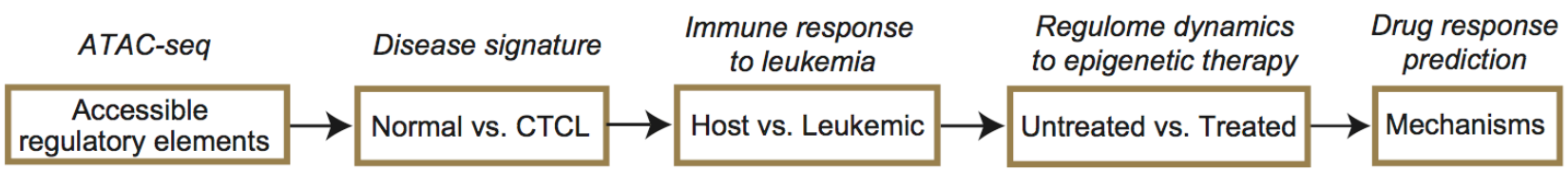


Central Dogma Video



T细胞淋巴瘤表观遗传调控机制研究

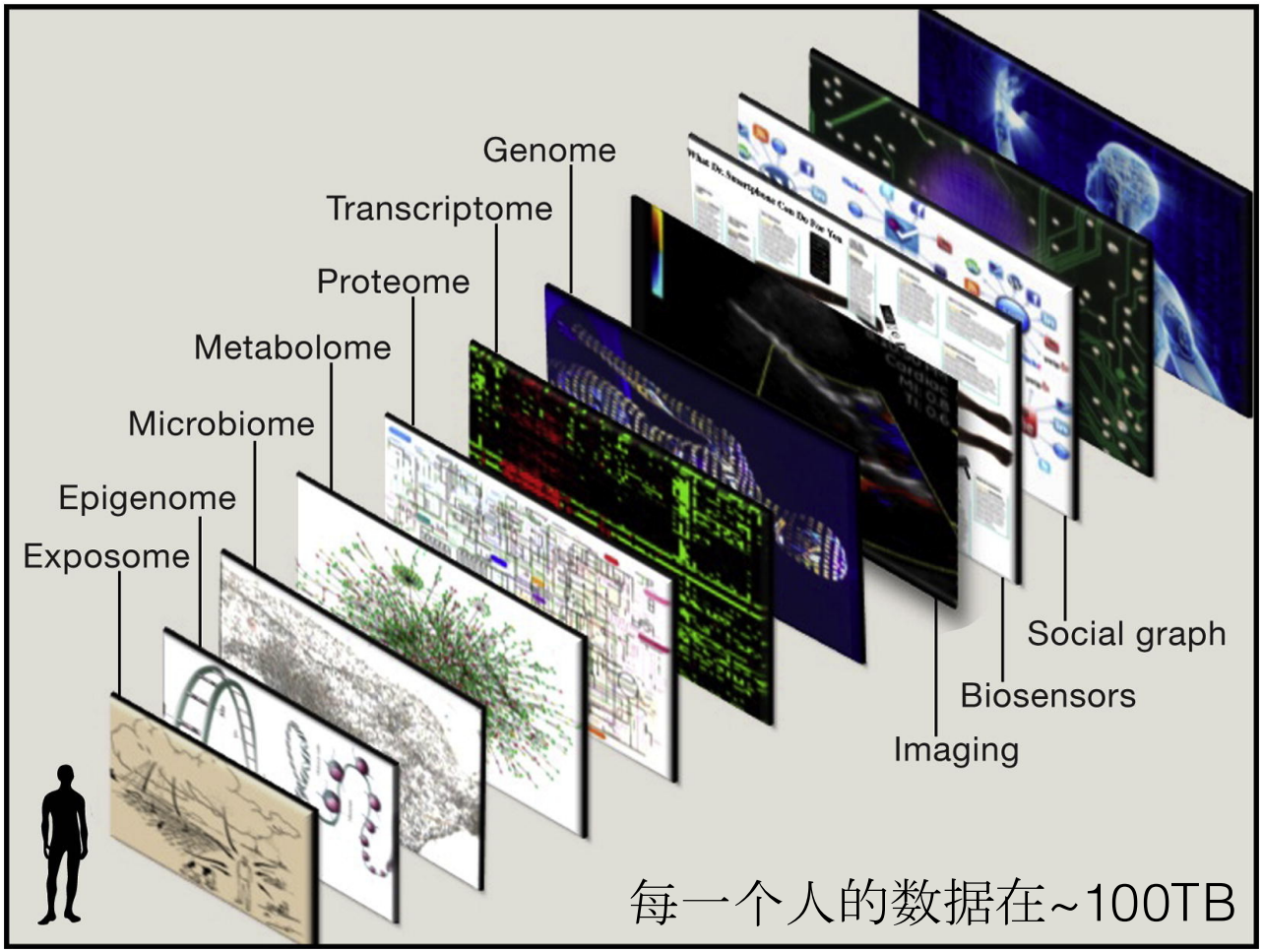




Cancer Cell, 2017

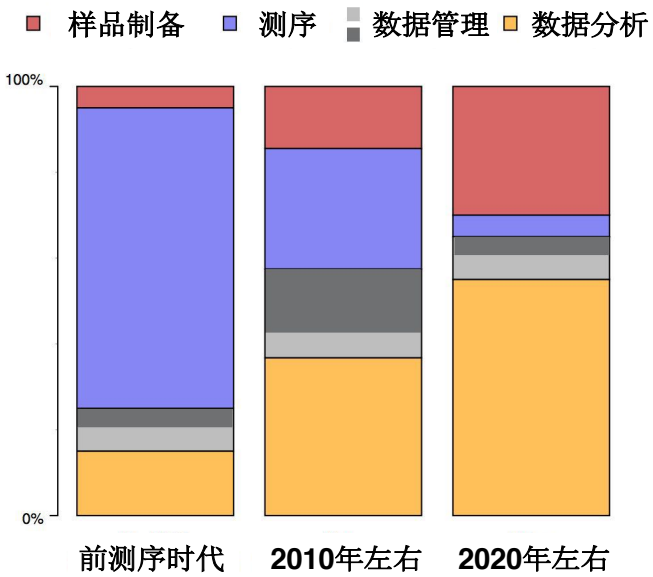
精准医疗，需要全面衡量对象的全部数据

对象的数据（包括但不仅限于）精准医疗2.0



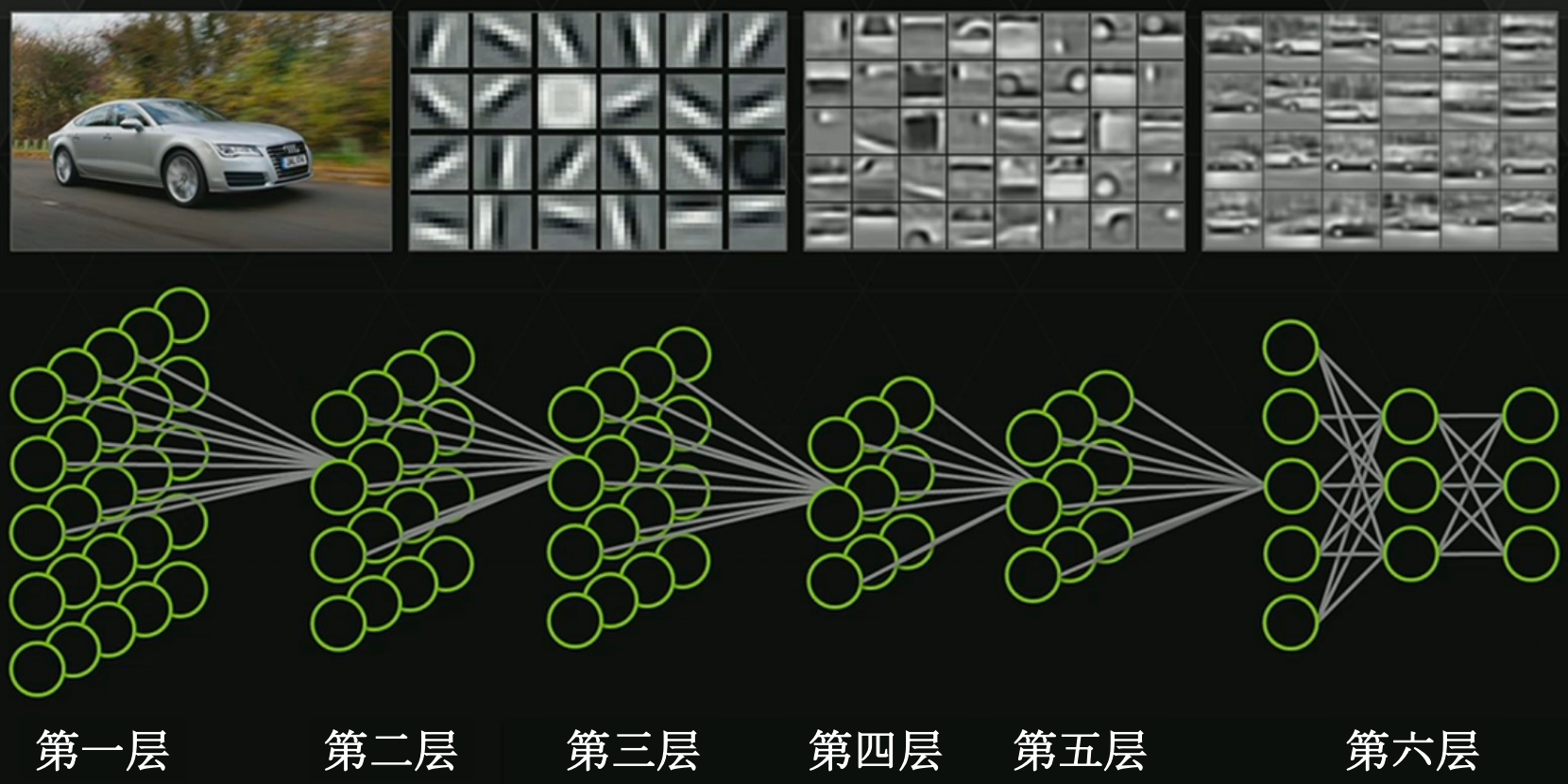
挑战将主要来自于数据解读

- 数据体量巨大
- 数据来源各异
- 数据类型复杂
- 数据格式不同
- 我们对数据本身的意义了解也不全面

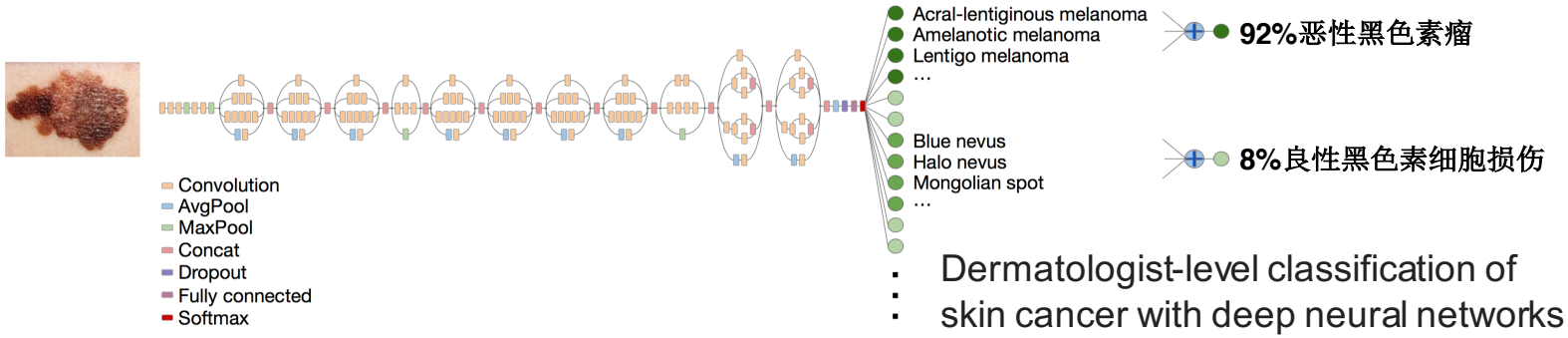


如何分析海量数据？
blue neurons / neu / January 2010.

HOW A DEEP NEURAL NETWORK SEES

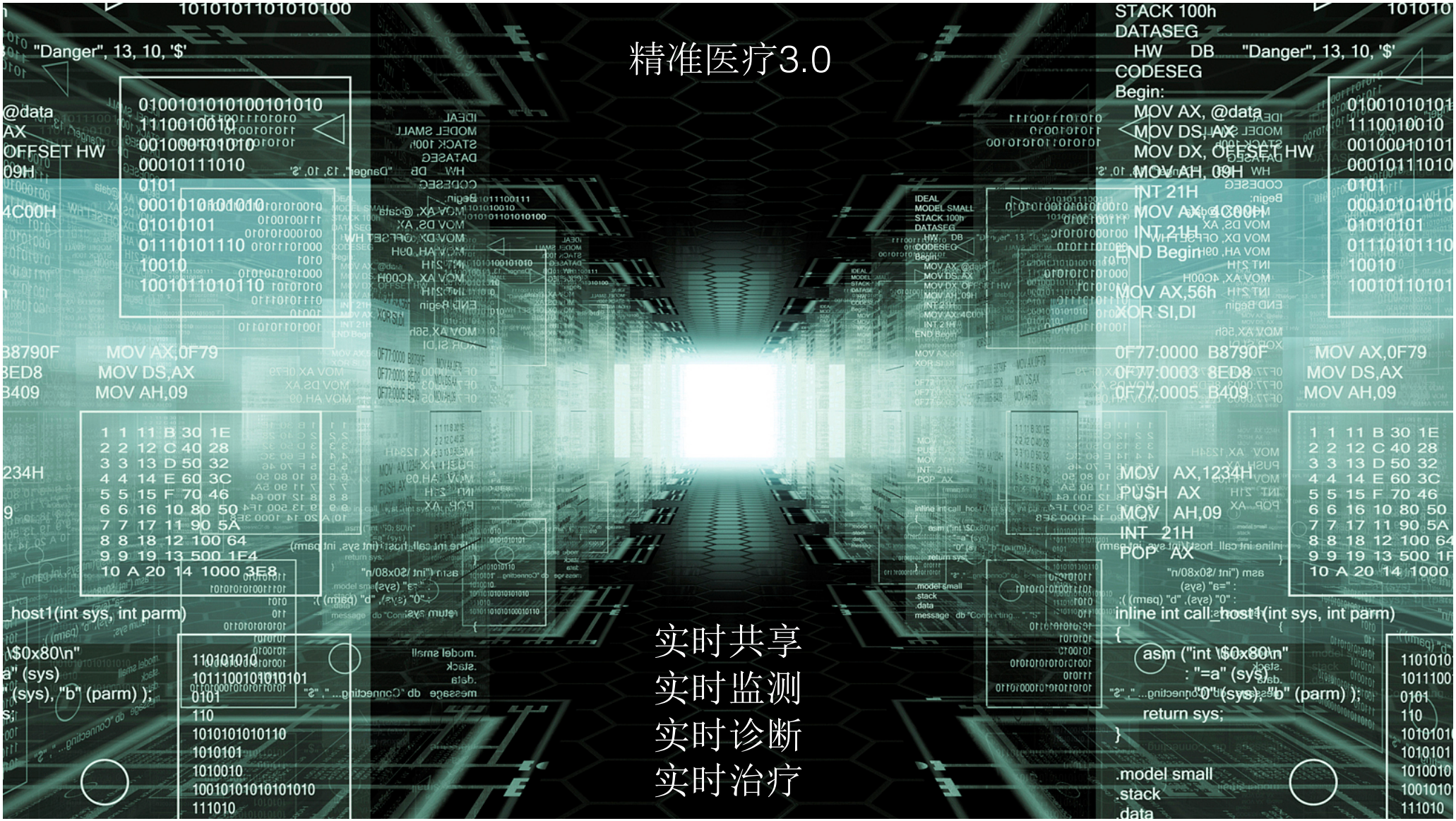


皮肤患处图片　　多重深度神经网络　　训练集　　概率预测



Dermatologist-level classification of skin cancer with deep neural networks

Nature, 2017


精准医疗3.0
实时共享
实时监测
实时诊断
实时治疗

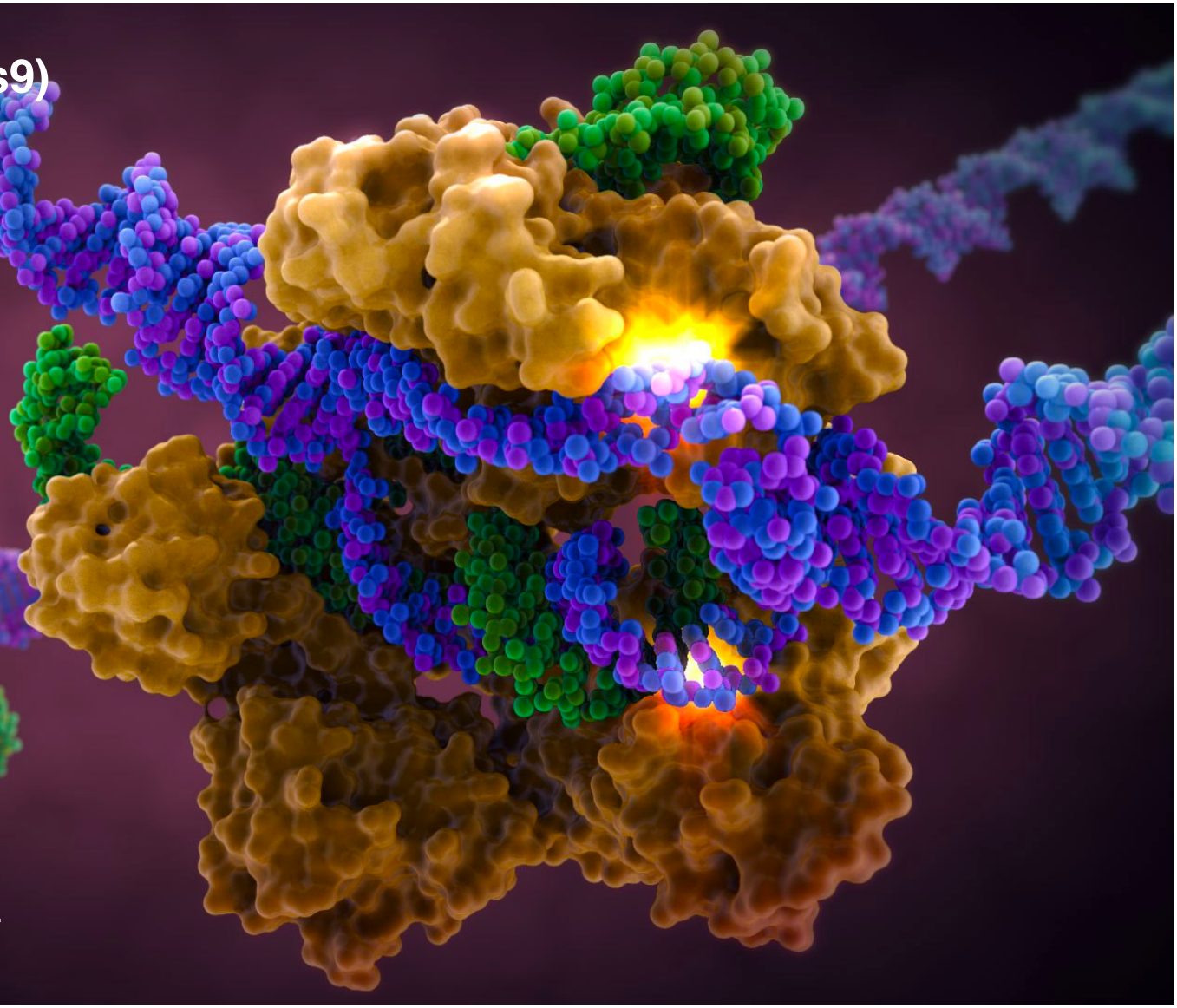
重新认识生物大数据和精准医疗

基因编辑技术(CRISPR/Cas9)

Feng Zhang

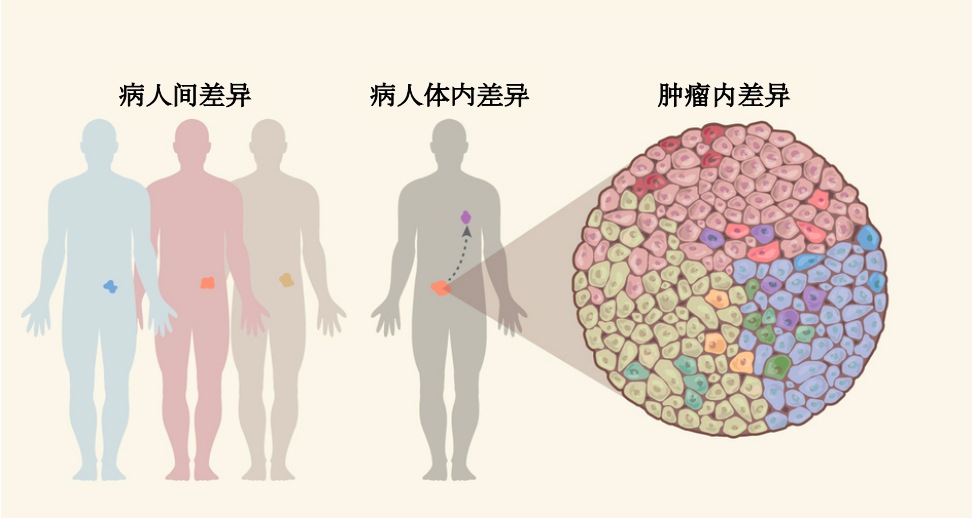
Jennifer Doudna

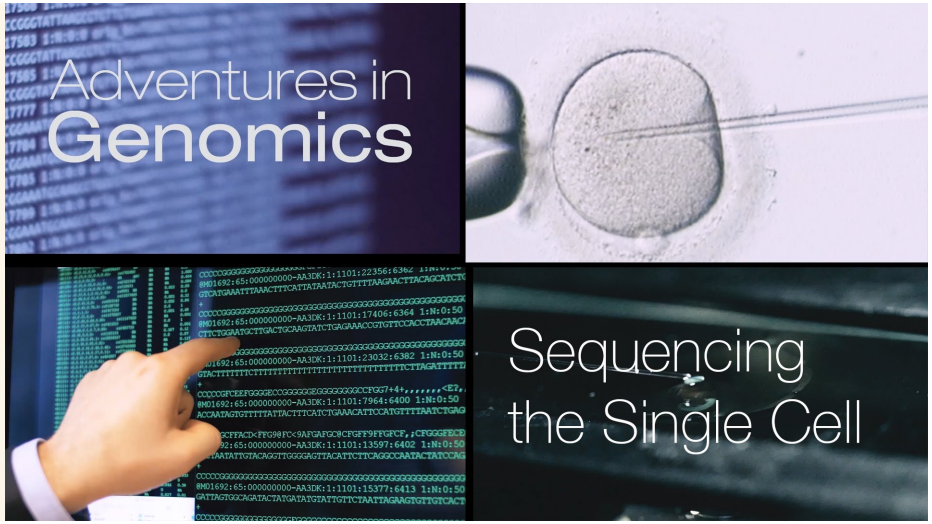
Emmanuelle Charpentier

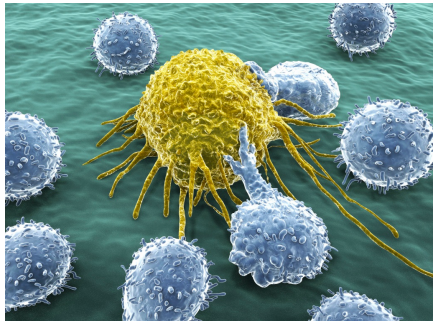


CRISPR Video

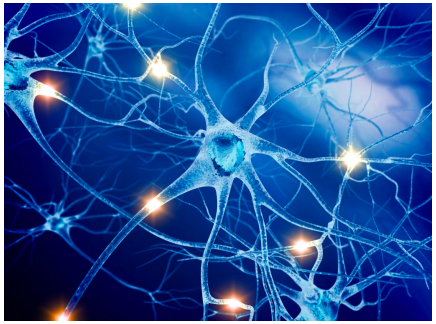
单细胞测序/基因组扩增技术



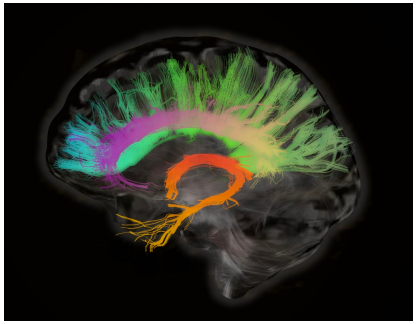




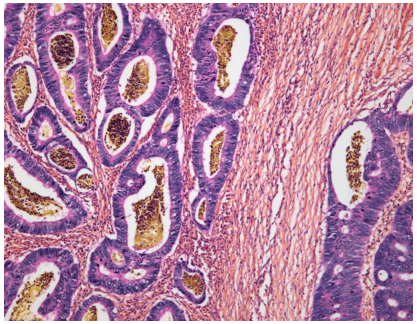
免疫细胞



神经元细胞



大脑细胞



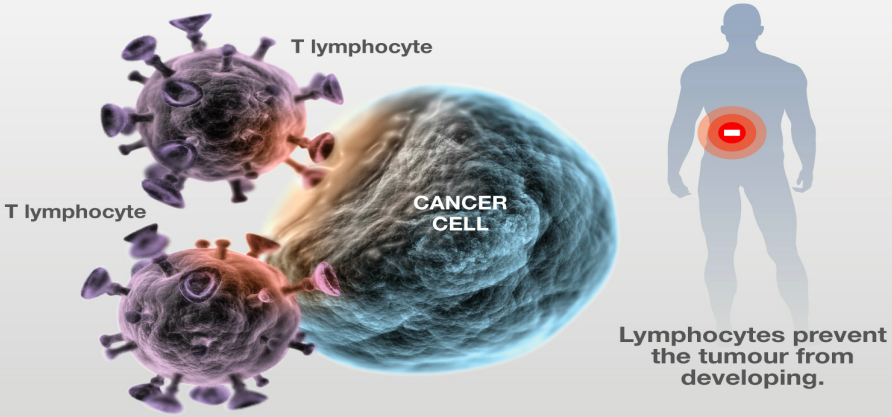
肿瘤细胞

Single Cell Sequencing Video

This is how the new immunotherapy for cancer works

1. Normal work of the immune system

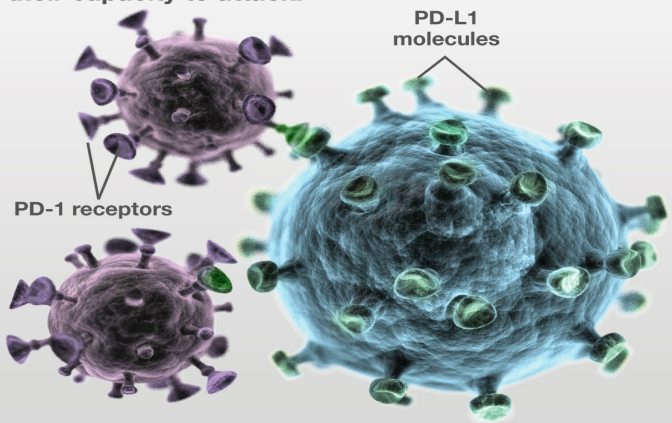
T lymphocytes are the cells of the immune system that identify tumour cells and destroy them.



Lymphocytes prevent the tumour from developing.

2. Camouflage of tumour cells

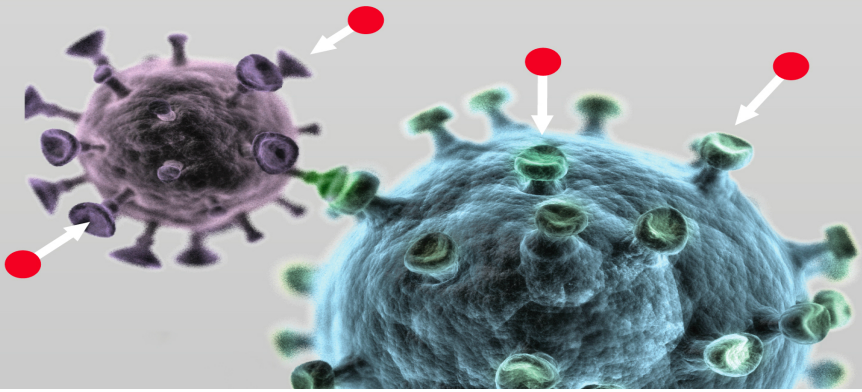
Some tumour cells arm themselves with a shield of molecules called PD-L1. Lymphocytes possess PD-1 receptors which, by bonding to these traps, destroy their capacity to attack.



The tumours become invisible to our defences and they spread.

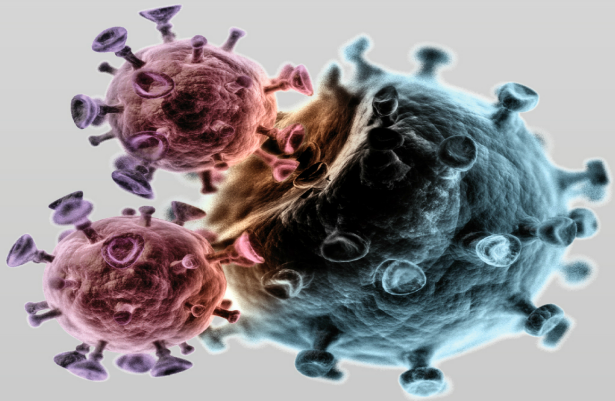
3. Action of the new inhibitor drugs

The new drugs based on antibodies block PD-1 from the cells of the immune system and PD-L1 from tumour cells to prevent their fatal action.



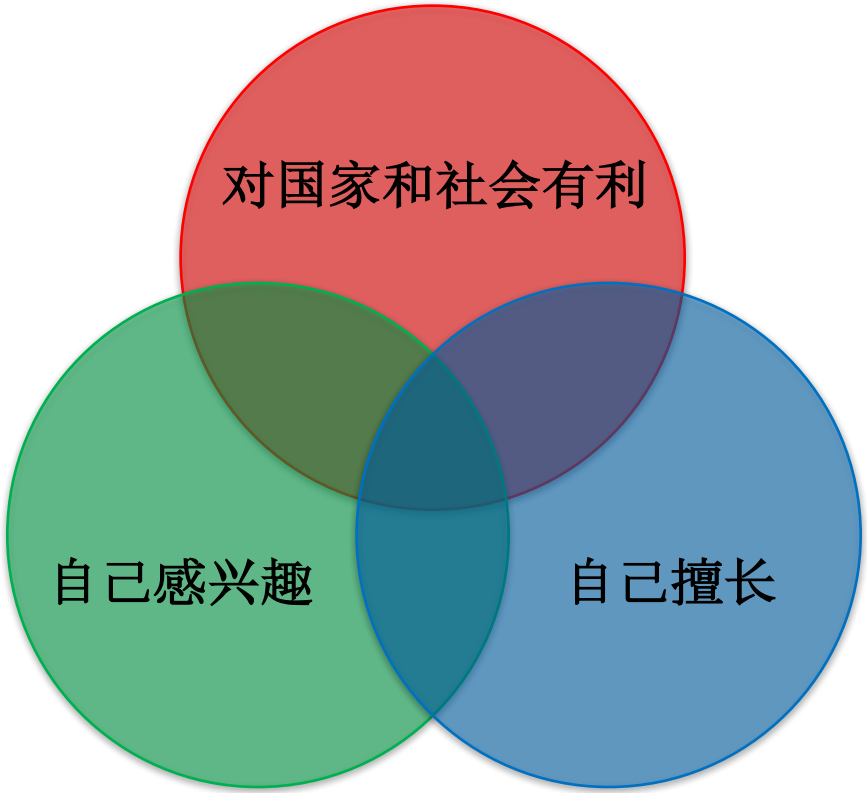
4. Result of immunotherapy

Lymphocytes, once freed from their blindness by the drug, regain their defence potential. They recognise cancer and reduce it.



This treatment, although still in its experimental stage, has had preliminary results on lung, kidney and skin cancers.

Cancer Immunotherapy Video



天才之为责任

Resources

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Cell Phone: 156-5697-5852
Address: 科大中区医学楼308

Course PDF: http://qulab.ustc.edu.cn/teaching/index.html