

# Biotech and early drug development in immunotherapy in China

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# **Clinical trials Worldwide**





# **Phase I trials Worldwide**







## Un-met needs for Development of Anti-Cancer Drug in China



300M cancer patients in China drive the big market of anti-Cancer Drugs

#### Anti-cancer drugs

Mono-Antibody drugs



http://m.biodiscover.com/news/industry/106268.html

Un-met needs for Development of Anti-Cancer Drug in China





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## Composition of different indication IND Application in 2011 to 2012





- China Drug Review Annual Report

# 2014 IND Application in China







- China Drug Review Annual Report

## **Application for Innovative Oncology drug**



## Domestic innovative Oncology drug application in 2008-2012 (Categories)



- China Drug Review Annual Report

# **Immune Research in China**



With the tremendous increase of funding from the National Natural Science Foundation of China, the Ministry of Science and Technology, the Ministry of Health, as well as regional governments in past years,



Between 2001 and 2011, the number of publications from China in the field of immunology rose from ranked fifteenth (in 2001–2005) to sixth (in 2006–2010).

X.T. Cao Nature Immunology 2008

# **Cancer Immunotherapy**



- 1. Cancer immunotherapy is a novel and promising new way for cancer treatment.
- 2. Top Breakthrough of the Year 2013 in Science
- 3. Cancer immunotherapy methods include:
  - Immune checkpoint inhibitor antibody
  - Adoptive cell therapy (DC-CTL, TIL, TCR, CAR-T)
  - Cancer vaccines: peptide, protein, DNA

## Immuno-Check Point and Chinese philosophy



In the traditional Chinese medicine theory, Yin (negative regulation) and Yang (positive regulation).





By controlling immune responses, immuno-Check point system can benefit the host by eliminating invading pathogens while not causing damage to host tissues.

# Immune checkpoint inhibitors in China





### **CTLA-4** inhibitors

### PD1 or PDL-1 inhibitors

PD-L1 expression in tumor tissue samples and its correlation with recurrence free survival in NPC





Fang WF, Zhang L et al: Oncotarget 2014

# LMP1 mediated the up-regulation of PD-L1 expression in EBV-infected human NPC cells



#### Fang WF, Zhang L et al: Oncotarget 2014

# Two mechanisms of up-regulated PD-L1 expression on EBV positive nasopharyngeal carcinoma cells





Fang WF, Zhang L et al: Oncotarget 2014



- CheckMate 077: CHECK point pathway and nivolu MAb clinical Trial Evaluation 077
  - A Phase 1/2, Open-Label Study of Nivolumab (BMS-936558) in
    Chinese Subjects with Previously Treated Advanced or Recurrent
    Solid Tumors
- CA 184247
  - A Phase 1 Dose Escalation Studyof the Safety, Tolerability, and
    Pharmacokinetics of Ipilimumab in Chinese Subjects with Select
    Advanced Solid Tumors

## **Adoptive Cell Immunotherapy**







3771

00-000-00

N=137

80

100

DC-CIK group

HIFN-α group

20

Control group

40

60

Time (months)

Chin Med J 2012;125(21):3771-3777



1.0

0.8

0.6

0.4

0

D. Hui et al. / Digestive and Liver Disease 41 (2009) 36–41

## **New Biotech and Cancer Immunotherapy**



### 华大基因研究院 BGI' research

- **Personalized immunotherapy** • Use next-generation sequencing result to guide personalized therapy
  - Whole Exome Sequencing
  - **RNA-seq**
  - TumorCare Sequencing Panel



- Oseq<sup>™</sup>-T Tumor Sequencing Panel
  - measure 508 tumor-related genes
  - \* Test sensitivity of 88 different tumor drugs

## **Peptide Vaccine Development for Liver Tumor**



#### Experimental Design



#### Exome Sequencing Result for Tumor Sample



#### Exome Sequencing Result



From outer to inner: Gene density, SNV, Transcript SNV, non synonymous coding SNV.

Anti-tumor effect of predicted peptide GPR55



(Li et al., submitted 2015, BGI)

#### **Immune Repertoire in Cancer Research**

#### **RESEARCH ARTICLE**

#### CANCER

#### Improved Survival with T Cell Clonotype Stability After Anti–CTLA-4 Treatment in Cancer Patients

Edward Cha,<sup>1</sup> Mark Klinger,<sup>2</sup> Yafei Hou,<sup>1</sup> Craig Cummings,<sup>2</sup> Antoni Ribas,<sup>3</sup> Malek Faham,<sup>2</sup> Lawrence Fong<sup>1</sup>\*

# The repertoire of clonotypes continued to evolve over subsequent months of treatment.

#### overall survival was associated with maintenance of high-frequency clones at baseline





Science Translational Medicine 2014



### The analytical pipeline in BGI - IMonitor



doi: 10.1534/genetics.115.176735 Genetics

SYSUCC

## **TCR repertoire analysis on HCC patients**



TCR repertoires of HCC patients are different from that of normal control

Yinxin Han et al., **Identification of characteristic TRB V usage in HBVassociated HCC by using differential expression profiling analysis,** Oncolmmunology <u>Volume 4</u>, <u>Issue 8</u>, 2015





- Big cancer patients pool drive the un-met needs for development of anti-Cancer drugs in China.
- Cancer immunotherapy will be more interesting treatment options for most solid tumor, especially for so-call: Chinese comment tumor type like liver cancer, esophageal cancer, gastric cancer, nasopharyngeal carcinoma
- Using new biotech like next-generation sequencing (NGS) result to guide personalized immunotherapy will be popular in the future.



# **THANK YOU!**

## Sun Yat-sen University Cancer Center

