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China Brain Project and non-human primate research in China

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Background

- **Two main funding agencies:**

  Ministry of Science & Technology (MoST)

  Natural Science Foundation of China (NSFC)

- **Proposa submitted on March 2015:**

  China Brain Project (2016-2030)

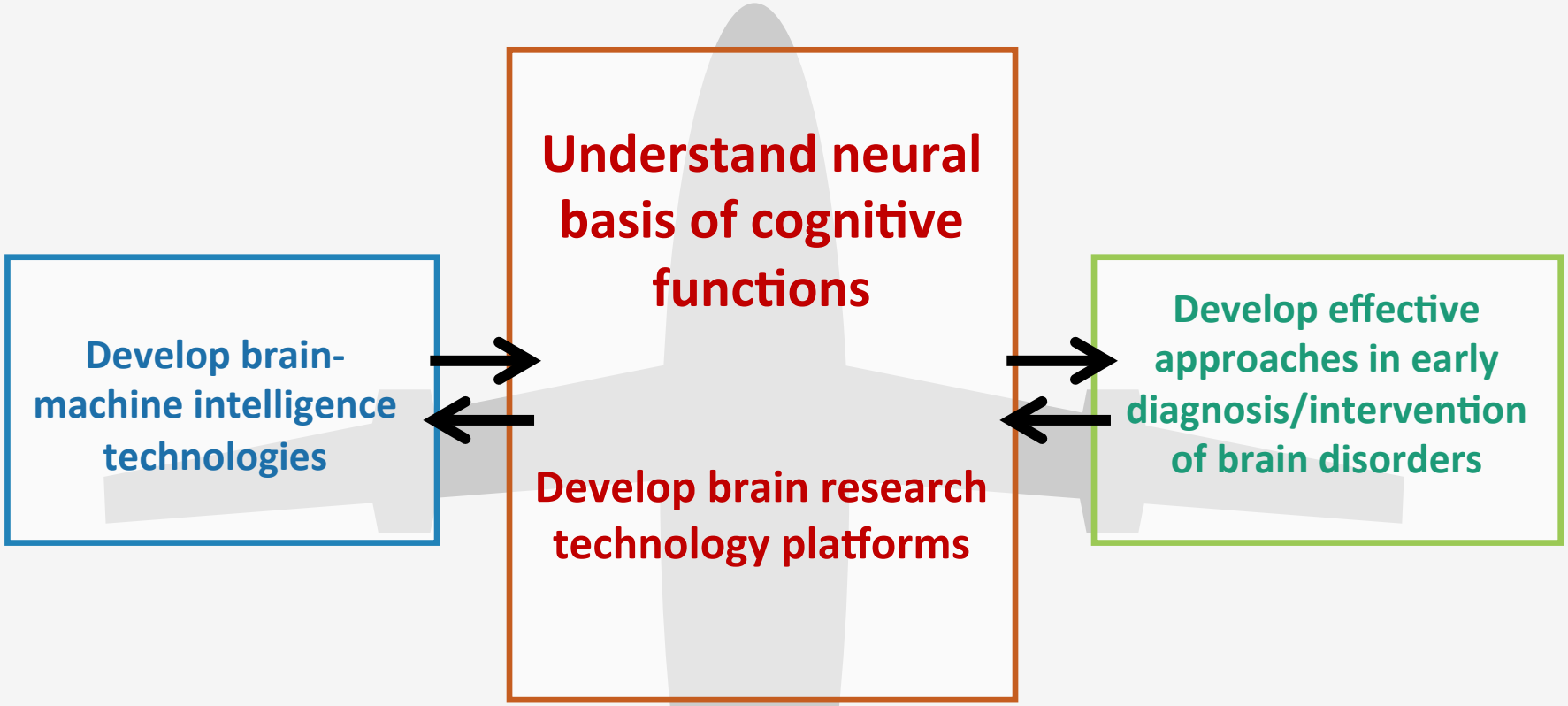
  "Brain science and Brain-inspired Intelligence Technology"

- **China Brain Project fo formally approved by the State Council in March, 2016，**
- **The budget and the funding mechanisms are yet to be announced**

China's brain research environment

- **Manpower (rapid increase of neuroscientist) :**
  - Home-grown talents and overseas returnees
  - Chinese Society for Neuroscience member ~6000 (doubling every five years)
- **Continuing increase of research funding**
  - Current R&D funding: 2.1% of GDP (goal: 2.5%)
- **Strong interdisciplinary supports**
  - Chemistry, physics, computer science, nanoscience, material science, engineering
- **Large populations of brain disease patients**
  - AD: 9M, PD: 2M depression: 30M, autism: >1M epilepsy: 9M
- **Abundant resource of non-human primates**
- **Tradition of social mobilization on a national scale**

China Brain Project — key objectives



"One body two wings (一体两翼)"

Building the core and developing the applications

Core component: Neural basis of cognitive processes

Approach: From Mapping to Understanding:

Mapping:

1. All cell types in all brain regions ("single–cell gene profiling")
2. Connections among all neurons in the brain ("connectome")
3. Activities of all neurons associated with specific functions

Understanding:

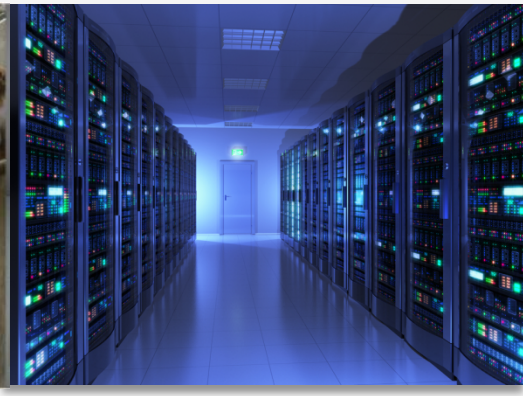
1. How genetic programs determine the building blocks of brains – molecules, cell types
2. How molecules and cells establish specific synaptic connections and generate specific circuit activities
3. How neural circuit activities generate cognitive brain functions and animal behaviors

Animal Models: Rodents and Macaque Monkeys

Basic brain technologies & platforms

- Single neuron gene expression profiling and labeling
- Circuit tracing technologies
- Brain imaging technologies
- *In vivo* electrophysiological and electrochemical recording
- Neuromodulation technologies
- Neural information processing platform
- Transgenic non-human primate platform



Applied component I:
Early diagnosis/intervention of brain disorders

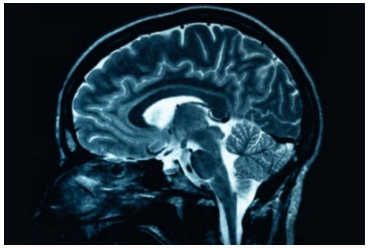
Focus on major brain disorders:

Developmental disorders (e.g., autism, mental retardation)
Psychiatric disorders (e.g., depression and addiction)
Neurodegenerative diseases (e.g., Alzheimer's and Parkinson's)

- Understand disease mechanisms
  - Genetic and epigenetic factors, pathophysiological circuit dysfunctions
- Develop early diagnostic tools
  - Genetic, molecular, imaging, and cognitive (functional) markers
- Develop early intervention approaches
  - Pharmacological, physiological and physical modulation
- Develop new disease models using non-human primates
  - Cynomolgus, rhesus, and marmoset

Clinical research platforms

- National database for brain imaging
- National blood-based biobank for brain disorders
- National brain bank
  (repository of healthy & diseased brains)
- National brain health training and education center



Applied component II:

Brain-machine intelligence technologies

- New generation of brain–machine interface and fusion devices
- Electrical, magnetic, ultrasonic neuro-modulation technologies
- Brain-inspired neural network models and computing methods
- Brain-inspired computing, processing, and storage devices
- Brain-inspired robotics

Monkey resources in China

(2012 Statistics, China Experimental Monkey Breeding Association)

Breeding companies: 40 (cynomolgus and rhesus monkeys)

Locations: Guandong、Guanxi、Yunan、Hainan、Sichuan

Total number in colonies: cynomolgus 250,000, rhesus 40,000

Total production in 2012: cynomolgus 60,000; rhesus, 10,000

Cynomolgus Monkeys
(*Macaca fascicularis)*

Rhesus Monkeys
(*Macaca muletta)*

Goals of non-human primate research in China

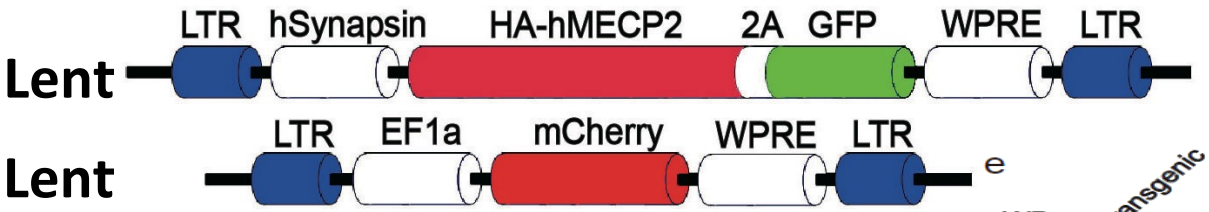
1. Studies of the cognitive functions using non-human primate as the animal model

2. Generation of genetically modified monkeys as animal models of human brain disorders and for basic neurobiology research

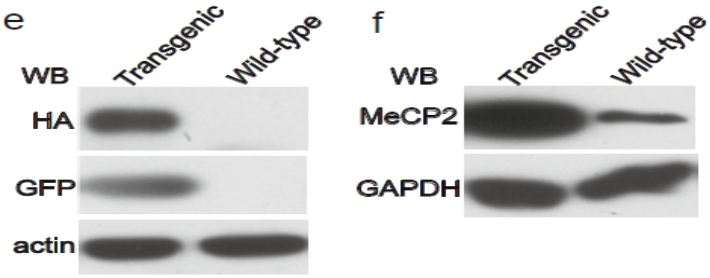
3. Development of training and education programs for sustainable research in primate neurobiology

4. Establishment of rigorous ethical practice in monkey research; public communication on the importance non-human primate research

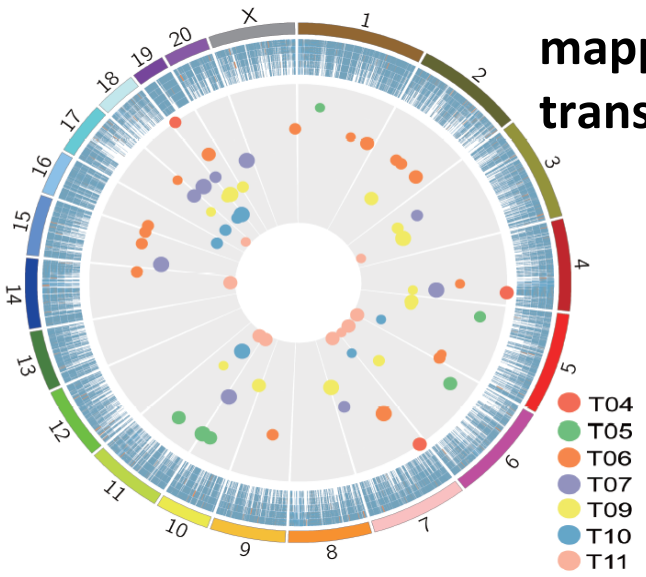
Lentiviral-based *MECP2* transgenic monkeys



neuronal-specific



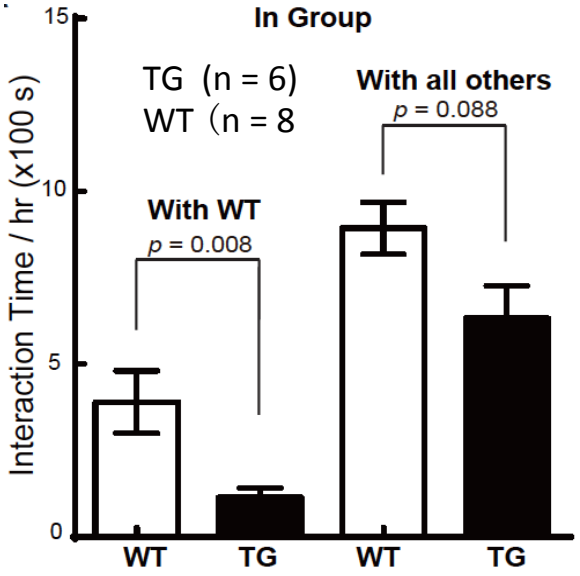
Liu et. al. Nature (2016)



mapping transgenes

No disruption of known exons by transgenes

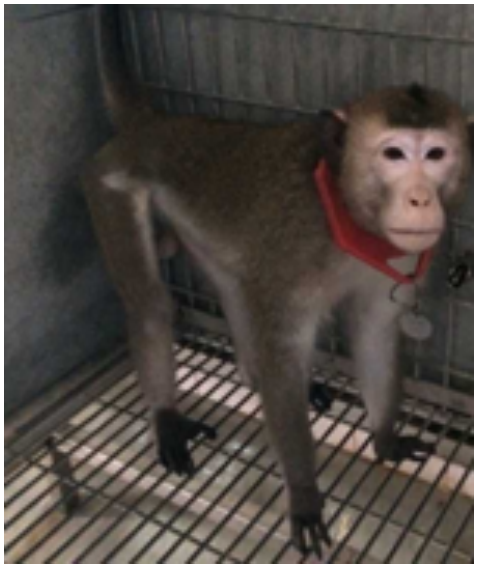
- ***MECP2* TG monkeys exhibit autistic phenotype**
  - ***Increased repetitive movement***
  - ***Abnormal social interactions***
  - ***Elevated stress responses***
  - ***Signs of stereotypic cognitive behaviors***
- **Ongoing structural and functional brain imaging for comparing transgenic and wildtype monkeys**



Acceleration of sperm maturation by testicular xenografts

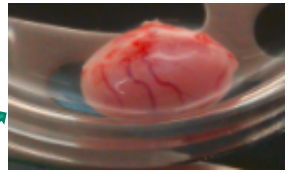
newborn

natural
sexual maturation
(4 - 6 years)

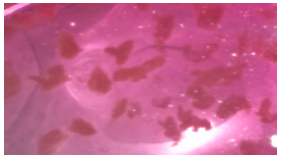


mature sperms for
intracytoplasmic
injection

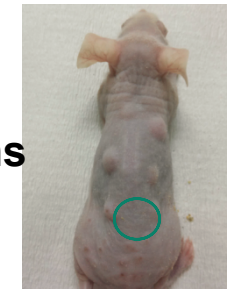
one year

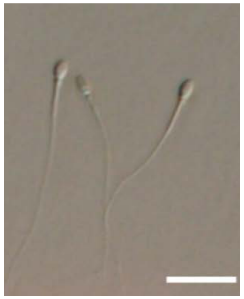


testis



11 months



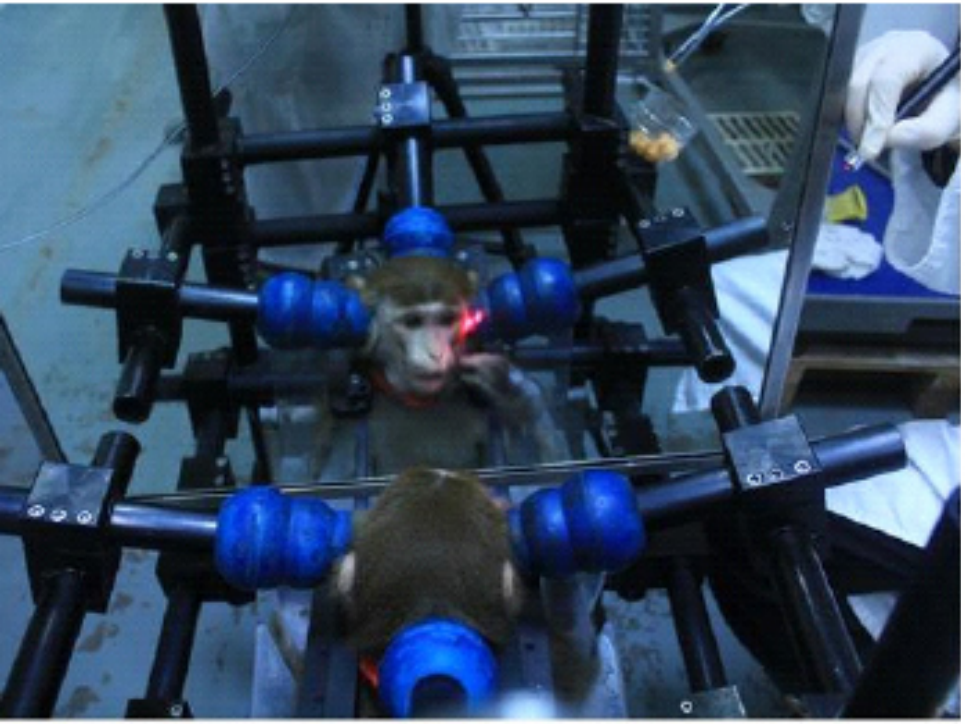


Liu et al. Cell Res. (2016)

testicular tissue pieces for
subcutaneous xenografting in mice

Reduction of generation time from 5 – 6 years to 2.5 years

Mirror self-recognition in monkeys



1. Rhesus monkey can learn mirror self-recognition following extensive training with visual-somatosensoy association
2. Brain imaging studies of monkeys before and after training are ongoing

*Chang et al. Current Biology (*2015)

Thank you!