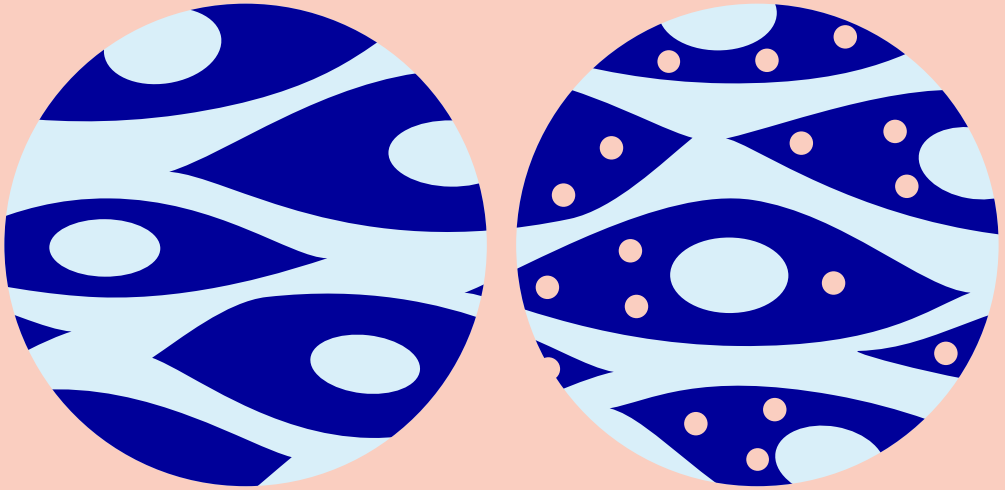
evotec

DDin
DRUG DISCOVERY INSIGHTS

EVOTEC AND CELGENE ENTER INTO DRUG DISCOVERY COL-LABORATION FOR NEURODEGENE-RATIVE DISEASES

Exclusive broad R&D collaboration based on Evotec's iPSC platform



iPSCs – A paradigm shift in drug discovery

Evotec's industrialised iPSC-infrastructure represents one of the largest and most sophisticated iPSC-platforms in the industry

Mission

- Develop novel therapies for a broad range of neurodegenerative diseases, based on Evotec's unique patient-derived drug screening platform induced pluripotent stem cells ("iPSCs")

Background

- The burden of neurological disease will remain a serious threat to public health
- iPSC-based models enable direct studies of human disease in a "dish"
- Vast majority of drugs do not address underlying causes
- Mostly poor (symptomatic) treatments that have been marketed for years

Agreement with Celgene

- Upfront payment of $ 45 m
- Potential milestones up to $ 250 m as well as up to low double-digit royalties on in-licensed programmes
- Initially five-year collaboration
- Focus on Amyotrophic lateral sclerosis ("ALS"), Alzheimer's disease ("AD"), Parkinson's disease ("PD"), and multiple other neurodegenerative diseases
- Celgene holds exclusive options to in-license worldwide rights to Evotec programmes developed from the company's compound library

evotec Celgene

OUR DEDICATED CORE IPSC TEAM

Expert scientists covering all aspects of iPSC-based drug discovery


SANDRA RAINER ANDREAS DAVE LEA


CARO MAREEN KIM HENRIK CORINNA


FATIMA YORK INA ANTJE SARAH


HEIKE NIKO CLAUDIA KARSTEN ANJA


ALEX MARK MANUEL HIRO JULIA


JASMIN SASKIA LENA ARIANA KRISTIN


BRUNO MATTHIAS GERALDINE AUDREY THERESA


NADINE STEFANIE CHRISTINA PIA SIMONE


DORIS PETRA HEIKE MEDHI PIERRE


ALEX HAUKE SABINE ANNELI THOMAS

NEURODEGENERATIVE DISEASES

Huge unmet medical need with
tremendous demand for new drugs

- **No cure** for most-known neurodegenerative diseases – Alzheimer's disease, Parkinson's disease, ALS (Lou Gehrig syndrome) or Huntington's disease
- No approved drug is able to stop disease progression or is tackling the root of the disease
- Alzheimer's disease – **No drug** available that can significantly **slow down** the progression of the disease
- For ALS there is just **one drug** approved, which has demonstrated to give a **2–3 month survival benefit** to ALS patients
- Currently there are **no approved drugs** for Huntington's disease, which could slow the deadly progression of the disease.
  ALS is deadly as well (even more quickly)
- Most effective Parkinson drug (Levodopa) was introduced in 1967

Global cost of care is approximately **$650 billion,** and expected to reach over **$1 trillion by 2030**

Increased clinical success rates are required to develop innovative drugs in this field

- Majority of CNS related clinical trials failed over the past 20 years due to limited or no efficiacy
- Between 2002 and 2012 413 Alzheimer's disease trials were performed with a haunting failure rate of 99,6%
- With comparably longer clinical development timelines and larger trials, sunk costs within CNS amount to multi-billion Euros per annum
- Many innovators have been leaving the neurodegenerative drug discovery field

EKIDEN TO IPS CELLS

Yamanaka likened his scientific career in terms of the iPS cell technology to an Ekiden.

"When I started a long ekiden — a relay marathon by multiple runners — toward cellular reprogramming about a decade ago, not many teams joined the start of the race."

"Owing to its simple and reproducible method, numerous laboratories around the world have started running in the ekiden ... I sincerely hope the technology will contribute to the development of new cures for people suffering from various diseases and injuries."

Shinya Yamanaka

Nobel Prize laureate for revealing that adult cells can be programmed
Source: Nature medicine, Volume 15 (10), 2009

"The use of patient-derived disease models for drug-screening represents a paradigm shift as it places the testing of human disease relevance at the front end of the drug discovery process and is expected to lead to the discovery of more disease relevant drug candidates but also more focused clinical development paths."

Dr Cord Dohrmann

CSO of Evotec

Why iPSC-based disease models?

- iPSC are made from adult specialised cells using a laboratory technique called reprogramming - that behave like embryonic stem cells
- Combining leading expertise in phenotypic screening, proteomics and iPSC handling provides a world leading platform
- Traditional pre-clinical CNS disease models are not predictive for humans
- iPSC-based models allow direct studies of human disease in a "dish"
- iPSC-based models allow early patient stratification
- iPSC-derived models provide superior translation to human disease and are expected to become a strong pillar of CNS drug discovery
- iPSC models are expected to accelerate pre-clinical development
- iPSC-based disease models will have a strong impact in most areas of discovery
- Phenotypic screens for modulation of disease phenotypes and underlying molecular pathways are expected to dominate future efforts
- Industrialisation of iPSC-based screening is still in its infancy

DID YOU KNOW?

FACTS ABOUT IPSC

IPSC CAN MAKE
ANY TYPE OF CELL IN THE BODY

THE FIRST ***IPS CELLS*** WERE MADE IN 2006. IT WAS THE WORK OF NOBEL LAUREATE ***SHINYA YAMANAKA*** AND COLLEAGUES – HE WON A ***NOBEL PRIZE*** FOR THE WORK IN 2012

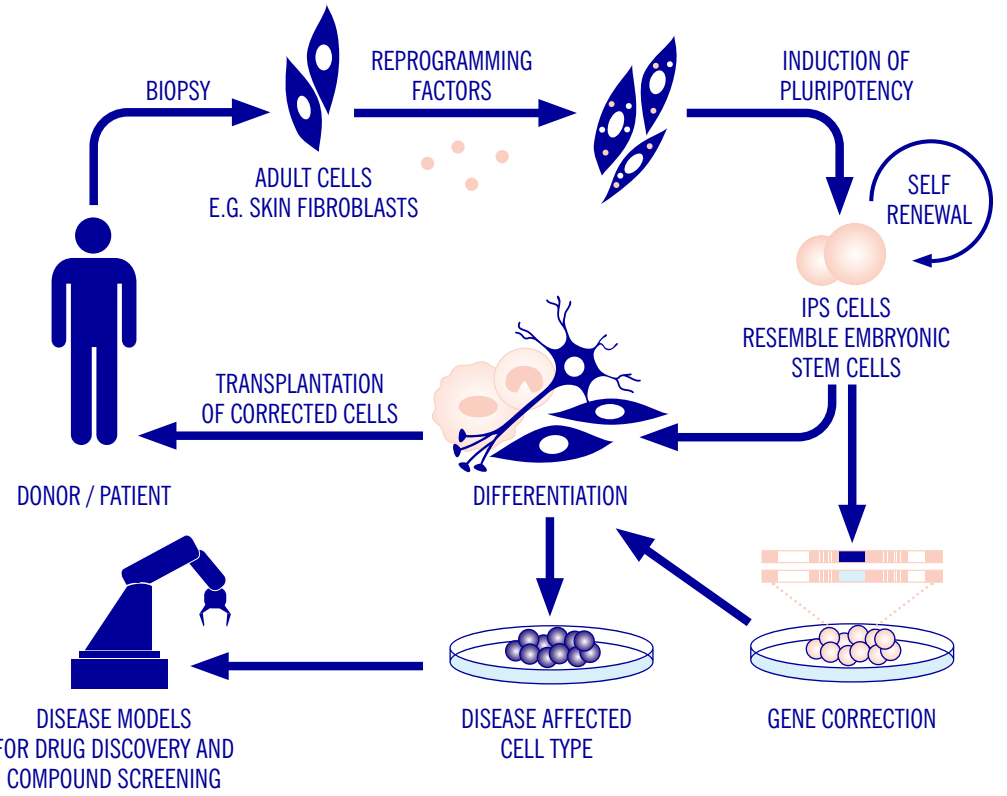
ADDING ***FOUR SPECIFIC GENES*** CONVERT ADULT CELLS INTO ***PLURIPOTENT STEM CELLS***

Pictograms by Noun Project users *(thenounproject.com)*: Oliviu Stoian *(Helix)*

FROM SKIN TO BRAIN

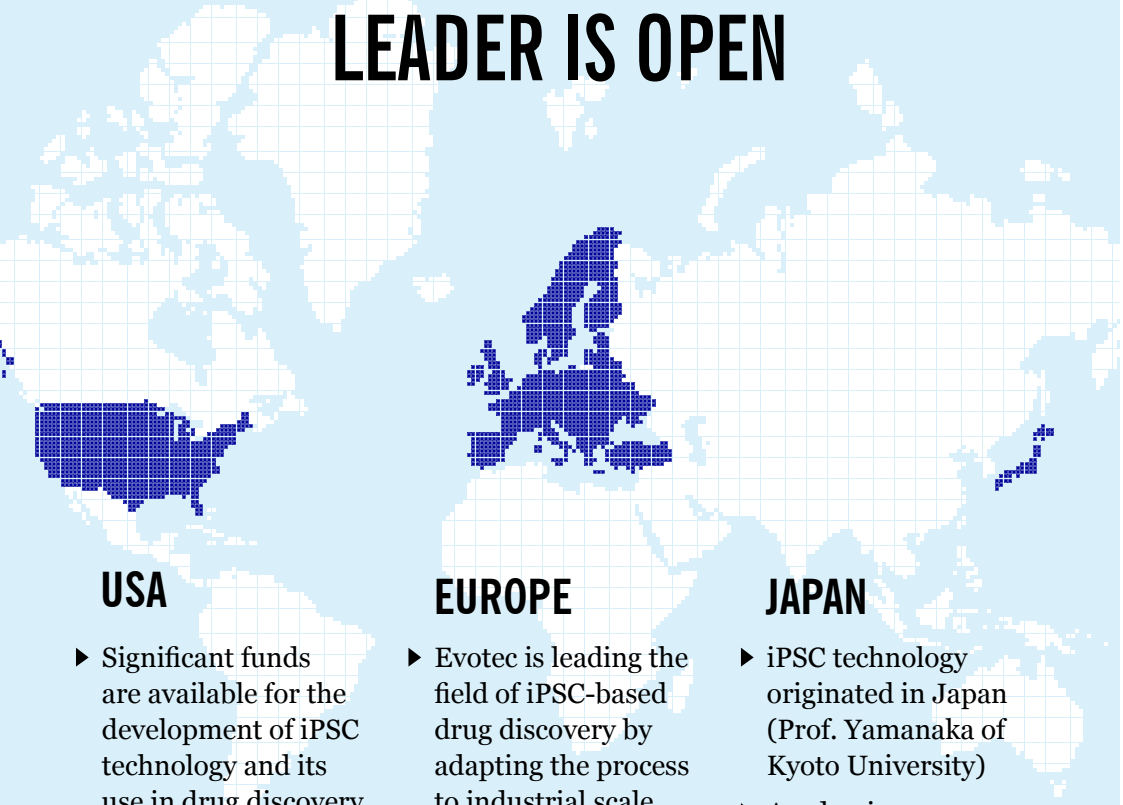
Discovery of iPSC in 2006 surprised many scientists and changed our thinking about how cells work.

Reprogramming has opened up exciting possibilities for studying and treating disease.



Source: www.eurostemcells.org

THE WINDOW OF OPPORTUNITY TO CREATE A EUROPEAN LEADER IS OPEN



USA

- Significant funds are available for the development of iPSC technology and its use in drug discovery
- A number of academic institutions have built up dedicated teams

EUROPE

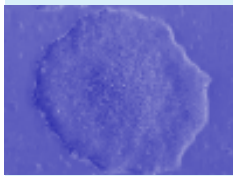
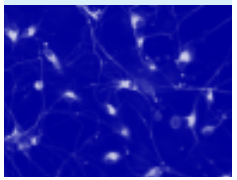
- Evotec is leading the field of iPSC-based drug discovery by adapting the process to industrial scale and robustness

JAPAN

- iPSC technology originated in Japan (Prof. Yamanaka of Kyoto University)
- Academia, large Pharma and biotechnology company have started further development of the technology

THE EVOTEC IPSC ACCELERATOR PLATFORM

Combining leading technologies are key to success

ACCESS TO PATIENT-DERIVED IPSC LINES	CUSTOMISED CELL-BASED ASSAYS	OPERA PLATFORM ORIGINALLY DEVELOPED BY EVOTEC	VERSATILE PROTEOMICS PLATFORM
iPSC	iPSC-based disease relevant assays	Phenotypic screening	MoA / cellular target profiling
▸ Banking ▸ Quality control ▸ Differentiation	▸ Disease modeling ▸ Adaption to high-throughput	▸ Small molecules ▸ Biologics	▸ Target deconvolution ▸ Biomarker identification
			

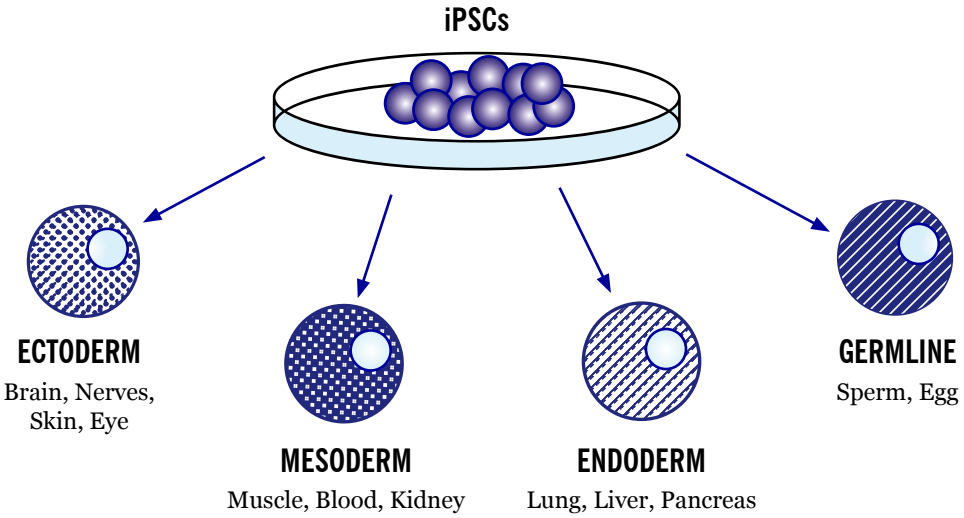
CureMN

Unique collaboration with Harvard Stem Cell Institute

Evotec's iPSC platform has been developed over the last five years with the goal to industrialise iPSC-based drug screening in terms of throughput, reproducibility and robustness to reach the highest industrial standards. That effort was enabled by a research collaboration and license agreement with Harvard University involving world-leading scientists at the Harvard Stem Cell Institute. In particular, a collaboration termed Cure*MotorNeuron* that was initiated in 2013 with the laboratories of Professors Kevin Eggan, PhD, and Lee Rubin, PhD, resulted in significant contributions to the platform. Additional aspects of the platform were built up through Evotec's more than 10-year collaboration with the CHDI Foundation in the field of Huntington's disease.

EVOTEC IS RUNNING MULTIPLE DRUG DISCOVERY PROGRAMMES USING IPSC

Neurological disease, retinal disease and diabetes



CORTICAL NEURONS
- HD (Huntington's disease)
- FTD (Frontotemporal dementia)
- AD (Alzheimer's disease)

INSULIN PRODUCING HUMAN BETA CELLS
- Diabetes

MOTOR NEURONS
- ALS (Amytotrophic lateral sclerosis)
- SMA (Spinal muscular atrophy)

DOPAMINERGIC NEURONS
- PD (Parkinson's disease)