ZF-screens

Christiaan Henkel
Leidse gracht
15 January 2013

ZF-screens

"Science, business and innovation; it's a delicate balance“

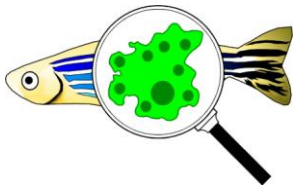
Dutch Life Sciences conference

Leiden

24 November 2016

Ron Dirks

CEO, ZF-screens BV



ZF-screens

- **Who are we?**
- What do we do?
- Where did the money come from?
- What do we want to do next?
- Where will the money come from?

ZF-screens

Dutch SME at Leiden Bioscience Park

- High-throughput drug and toxicity screens in zebrafish larvae
- Next generation sequencing (genomes, transcriptomes)

Chris Henkel
Leiden Univ

Herman Spaink
Leiden Univ

ZF-screens

- Who are we?
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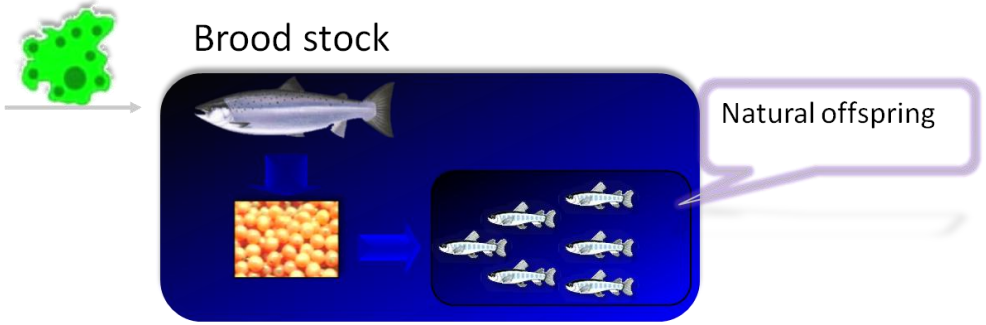
ZF-screens daughter 1

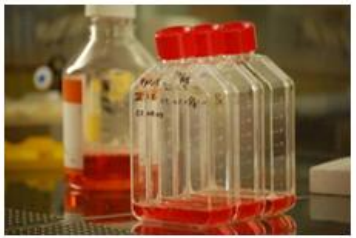
- Founded in 2007 (Herman Spaink and Guido van den Thillart)
- Artificial maturation of broodstock for aquaculture (European eel, pike perch, common sole, salmon)
- Main product: ZF-Implant™

NewCatch activity

ZF-implant™



- Artificial pituitary gland
- Living slow-release system
- Inject into parent fish (brood stock)
- Very few injections compared with weekly hormone injections



Quick help

- What is meant by high quality text as facsimile?
- What does A1, A2, A3 and B stand for after a European publication number?
- What happens if I click on "In my patents list"?
- What happens if I click on the "Register" button?

Bibliographic data: EP1686179 (A1) — 2006-08-02

In my patents list | EP Register | Report data error | Print

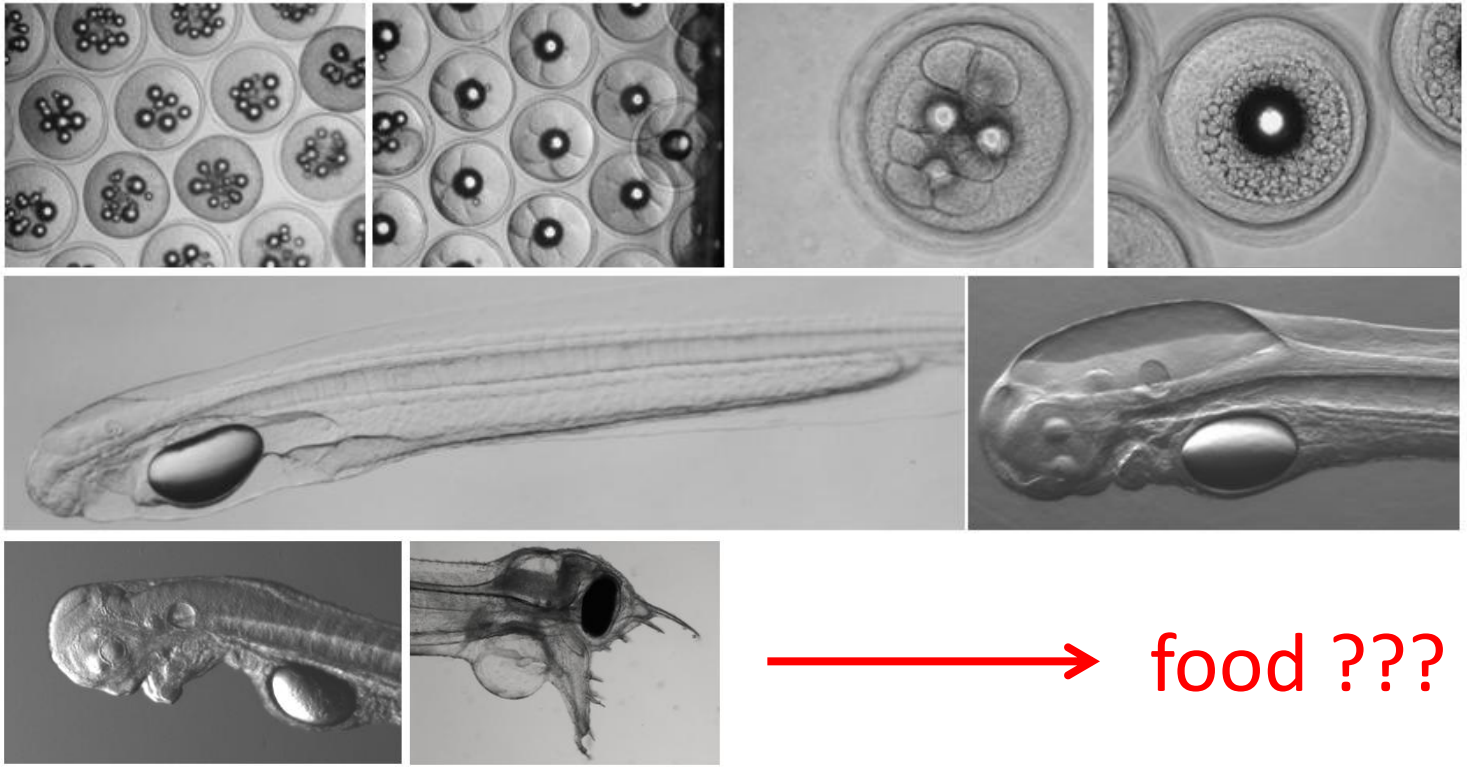
Means and methods for improving the development and maturation of eggs and/or sperm in fish using hormones produced by transplanted cells

Page bookmark	EP1686179 (A1) - Means and methods for improving the development and maturation of eggs and/or sperm in fish using hormones produced by transplanted cells
Inventor(s):	SPAINK HERMAN PIETER [NL]; VAN DEN THILLART GUIDO EVERAD [NL]; SCHNABEL PERAZA DENHI [NL] +
Applicant(s):	UNIV LEIDEN [NL] +
Classification:	- **international:** ***A01K61/00; C12N15/85***
	- **cooperative:** **A01K67/0271**; A01K2207/12; A01K2227/40; A01K2267/02
Application number:	EP20050075204 20050126 Global Dossier
Priority number(s):	EP20050075204 20050126
Also published as:	ES2348923 (T3) CN101180399 (A)

Facilities for reproduction trials

custom-adapted sea container

Eel larva development



ZF-screens daughter 2

ZF-pharma
ZF-screens company

- Founded in 2008
- High-throughput drug screening in zebrafish larvae
- Toxicity assays in zebrafish larvae

The zebrafish as a model organism

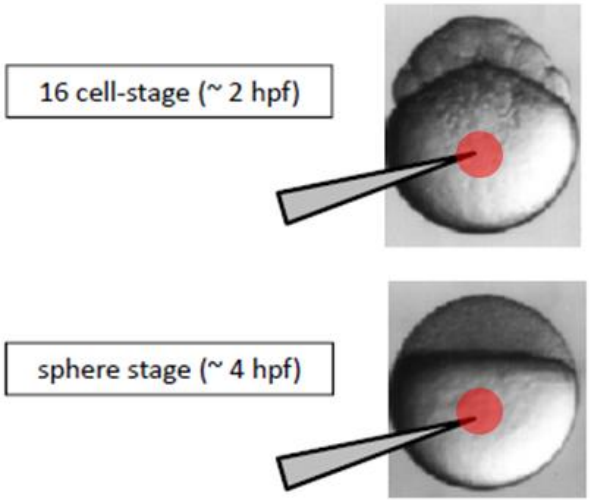
- Easy to culture
- Transparent larvae ideal for imaging
- Many transgenics for fluorescence imaging
- Excellent genomics tools available

ZF-pharma
ZF-screens company

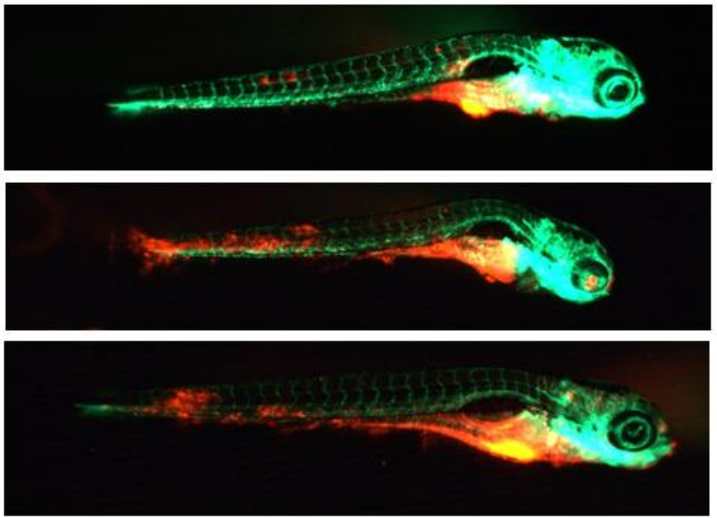
Invention 1: Yolk injection of microbes

Patent WO2011/005094 (publication date: 13 January 2011)
High throughput method and system for in vivo screening (H. Spaink and R. Dirks)

injection stage

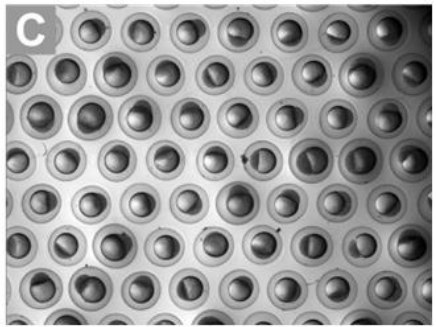


5 day old larvae with tuberculosis



Invention 2: Automated yolk injection of microbes

Patent WO2011/005094 (publication date: 13 January 2011)
High throughput method and system for in vivo screening (H. Spaink and R. Dirks)



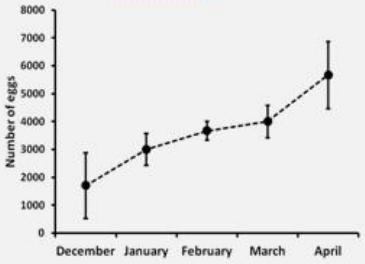
Collaboration with
Jan de Sonneville
(LifeScienceMethods)

ZF-pharma
ZF-screens company

High throughput drug screening in zebrafish; 7 day screening pipeline

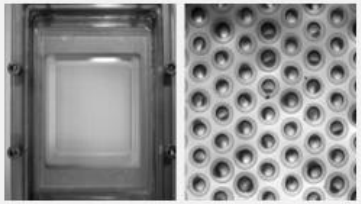
large-scale production of synchronized embryos

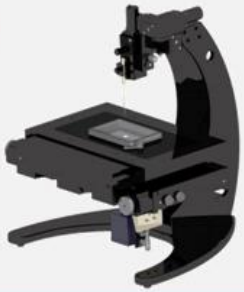
- iSPAWN

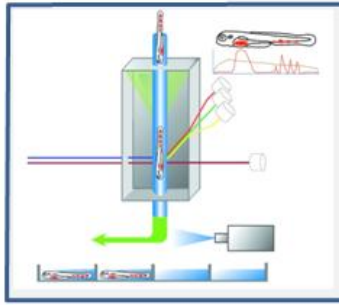


high-speed robotic intravolk injection of bacteria

- high speed and capacity
- automatic needle calibration
- optimized needles







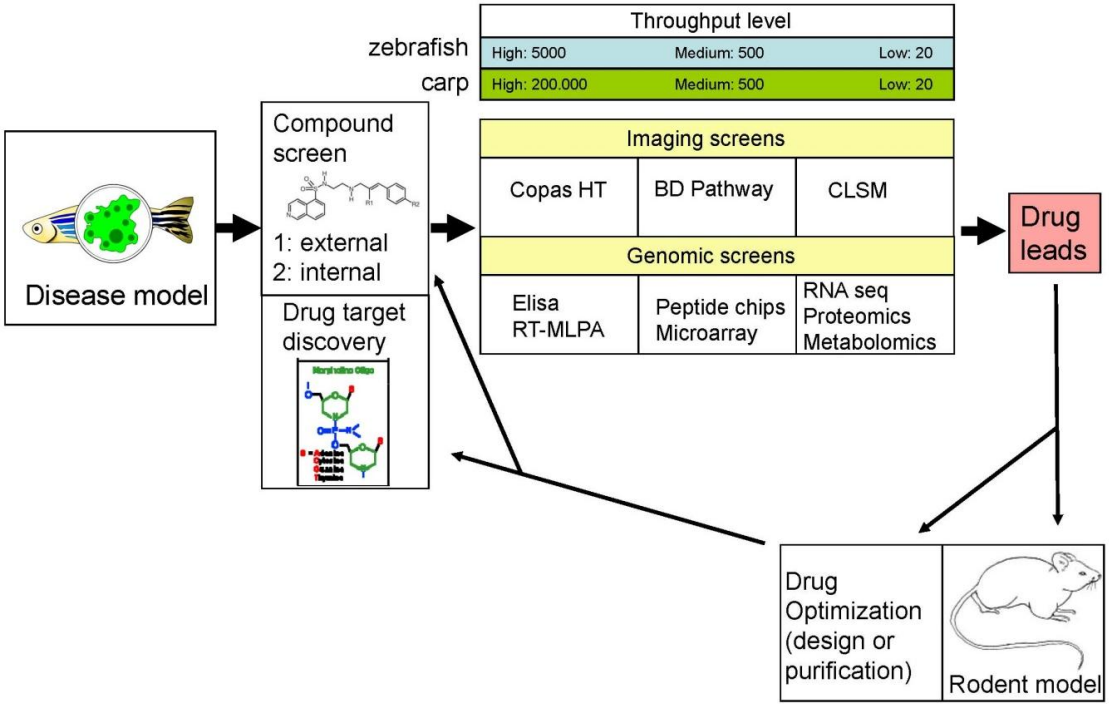
screening assays:
optimized COPAS
sorting protocols

- pre-sort larvae at 3 dpi to obtain homogeneously infected groups
- consecutive measurements at 4, 5, 6, 7 dpi

ZF-pharma
ZF-screens company

High throughput drug screening in zebrafish

zebrafish fills gap between cell culture and rodents



ZF-screens

- Who are we?
- What do we do?
- **Where did the money come from?**
- What do we want to do next?
- Where will the money come from?

- Financial resources until now:
  - National and European grants
    - e.g. SmartMix (ZF-pharma); LNV (NewCatch)
    - e.g. ZF-Tools (FP6), ZF-Cancer (FP7), FishForFharma (ITN)
  - Customers
    - pharmaceutical companies (infectious diseases)
    - service activities
      - Next generation sequencing
      - CRISPR/Cas9 zebrafish mutants

PreDiCT-TB (IMI project)

Model-based preclinical development of anti-tuberculosis drug combinations

5 years
28.9 M€

2 Post-docs 2 technicians

Consortium of 21 groups

Innovative Medicines Initiative: Public private initiative 2B€

European federation of Pharmaceutical Industries and Associations

European Union

ZF-screens

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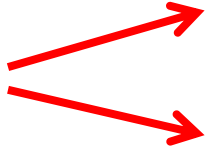
ZF-screens

- NewCatch (ZF-Implant)
  - quality high enough (massive production of hormone)
  - immunological rejection by host
  - high cost of product
  - activity stopped in 2015

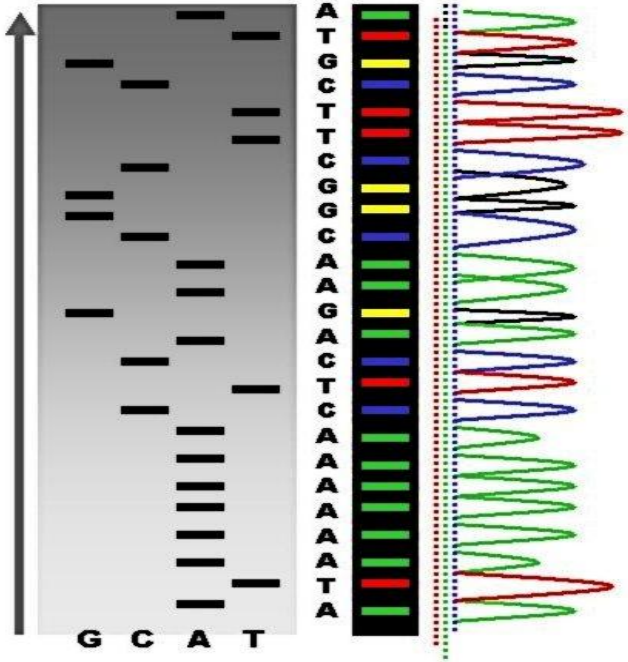


GLASAAL VOLENDAM

eelric
eel reproduction innovation centre

- ZF-pharma (in vivo drug screening in zebrafish)
  - complete screening pipeline needs 7-day-old larvae
  - 2015: new strict EU and Dutch legislation
    - only 5-day-old larvae allowed → activity stopped in 2016

First generation sequencing



source: wikipedia

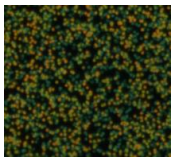
"dideoxy" or "Sanger" sequencing (1977)

- (capillary) electrophoresis
- reads length up to 1,000 nt

Human Genome Project (1990-2003)

- ~ 3.3 billion nucleotides
- ~ 3 billion US Dollars

Second generation sequencing



“massive parallel” or “Illumina” sequencing (Roche 454, Solid) (~ 2006)

- sequence millions of fragments simultaneously
- microscopy
- read length up to ~ 250 nt
- 600 Gb per day

Giant Panda Genome Project (Li et al., 2010, Nature 463, 311-317)

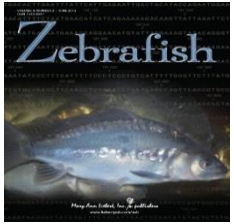
- first vertebrate “Illumina only” project

ZF-screens

genome projects at ZF-screens

European eel
PLoS ONE, 2012

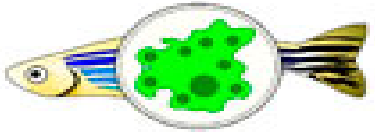
Japanese eel
GENE, 2012



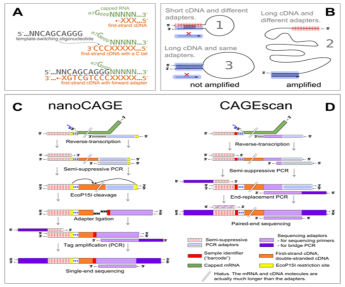
Common carp
Zebrafish, 2012

King cobra
PNAS, 2013

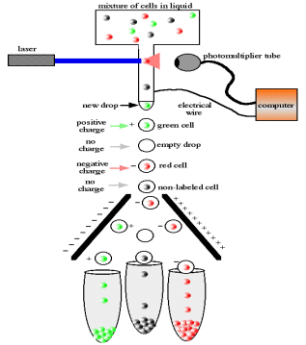
transcriptomics projects at ZF-screens



multiple regular mRNA-seq projects (mostly zebrafish)



NanoCage sequencing

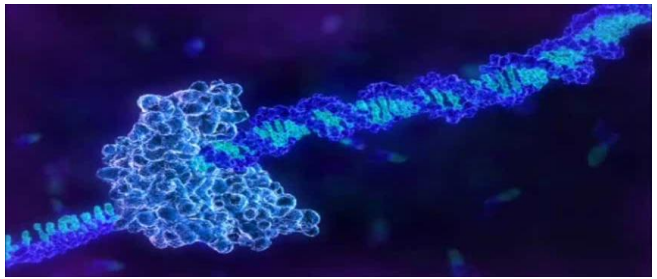


FACS-sorted cells

Single molecule sequencing (SMS)

(third generation sequencing)

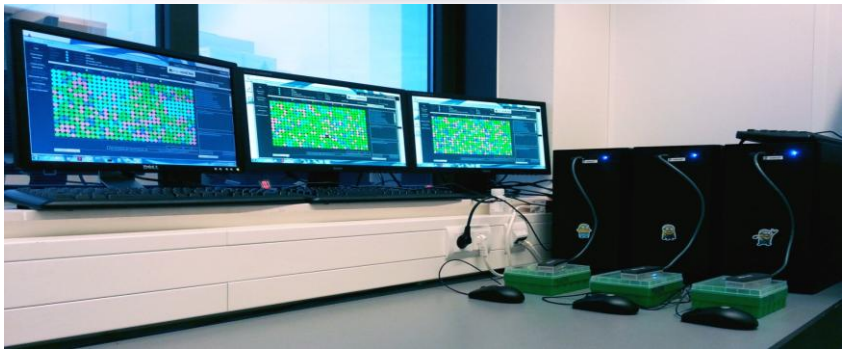
- Pacific Biosciences



De novo genome assembly with long reads via Nanopore sequencing

Oxford Nanopore Technologies; http://www.nanoporetech.com

MinION



PromethION

available by December 2016

predicted output: 6 Tb per day!!!

ZF-screens

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- **Where will the money come from?**

- Future financial resources:
  - Service activities
    - Genomics projects
    - Zebrafish larvae Tox projects (up to 5 days)
  - Customers
    - Industry
    - Academia
    - Hospitals
  - Grants (genomics)
    - e.g. Horizon2020: ParaFishControl

- Summary
  - Continuous product innovation
    - ZF-implant (2007 - 2015)
    - Zebrafish screening pipelines (2008 - 2016…)
    - Next generation sequencing (2009 - …)
  - Continuously changing financial landscape
    - financial crisis (extremely careful banks)
    - investors (short term return on investment)
    - changing national and EU grants
      - from academic to nearly commercial projects

Thanks for your attention