The Haplogen Story

@ Patentportfolio als Basis zum Geschäftserfolg

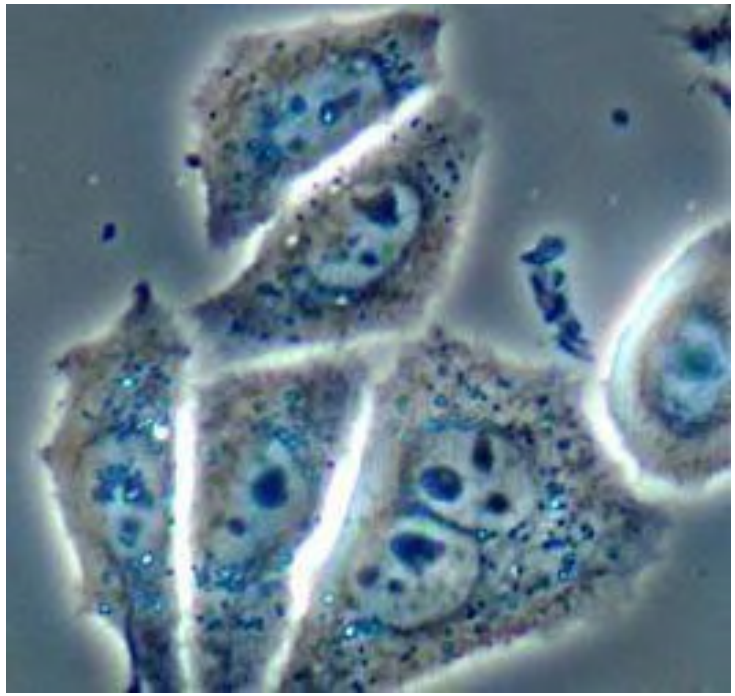
AWS, April 15, 2015

Georg Casari, CEO
Haplogen GmbH
Campus Vienna Biocenter 3
1030, Vienna Austria

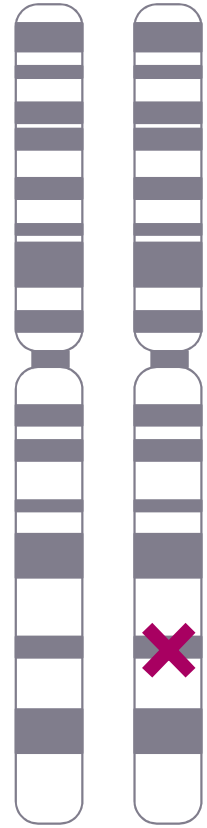
Phone +43-1-9165522
office@haplogen.com
www.haplogen.com

Was wünschen sich biomedizinische Forscher?

Genetics in human cells

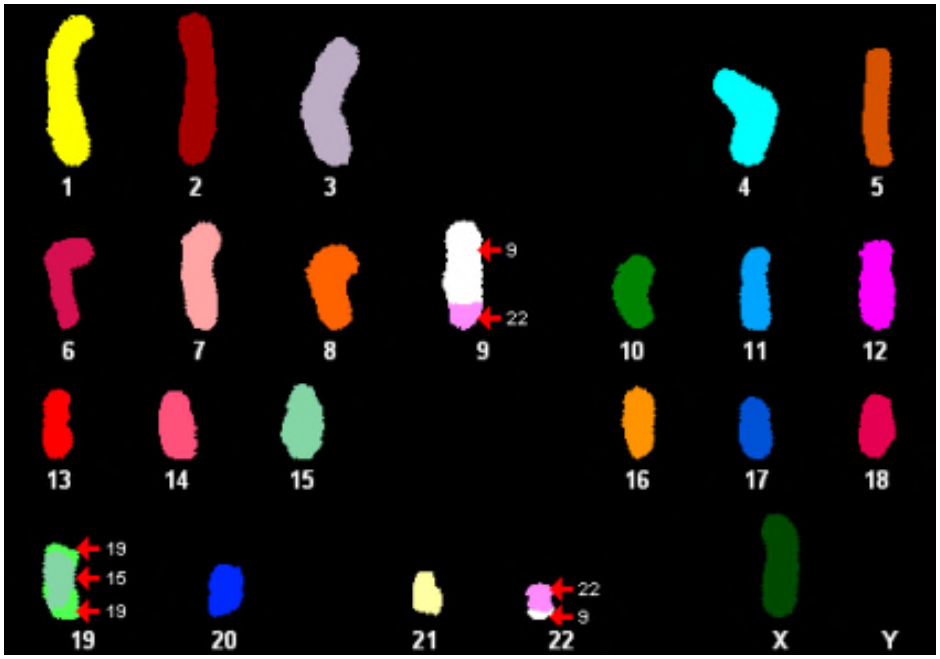


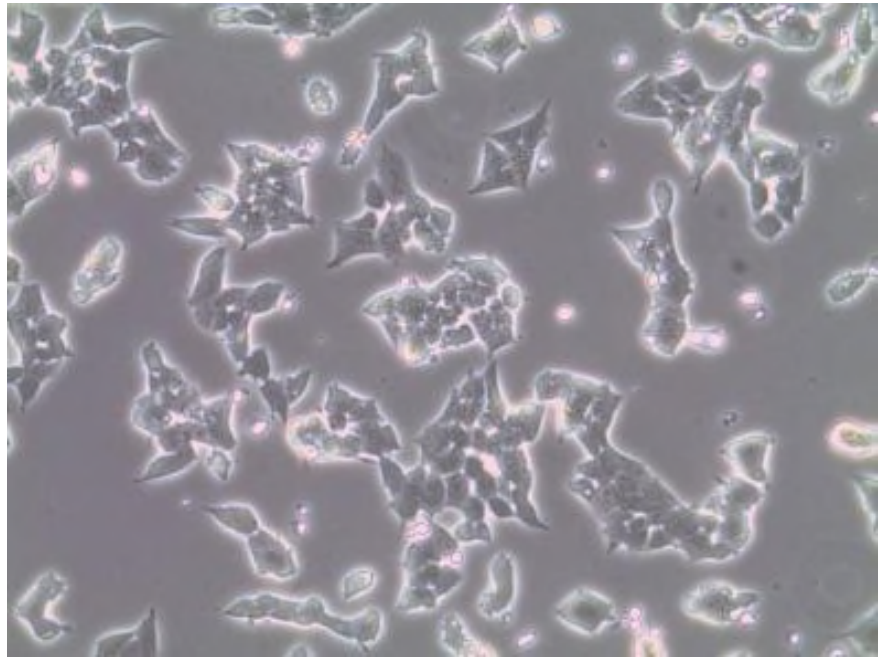
Major hurdle:



Mutation masked by second copy

Eine beinahe-haploide menschliche Zelllinie



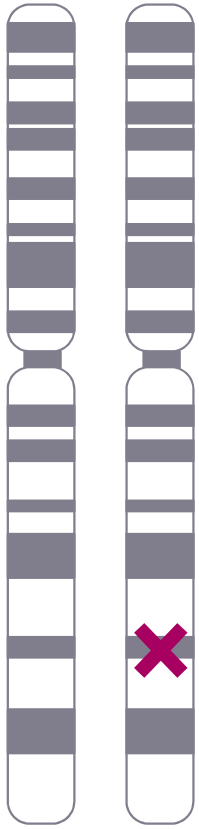


- Human
- Adherent fibroblast-like
- Almost fully haploid
- Well characterized

Carette et al. (2009) in *Science*
Carette et al. (2011) in *Nature*

Gene inactivation in diploid versus haploid cells

Diploid cells

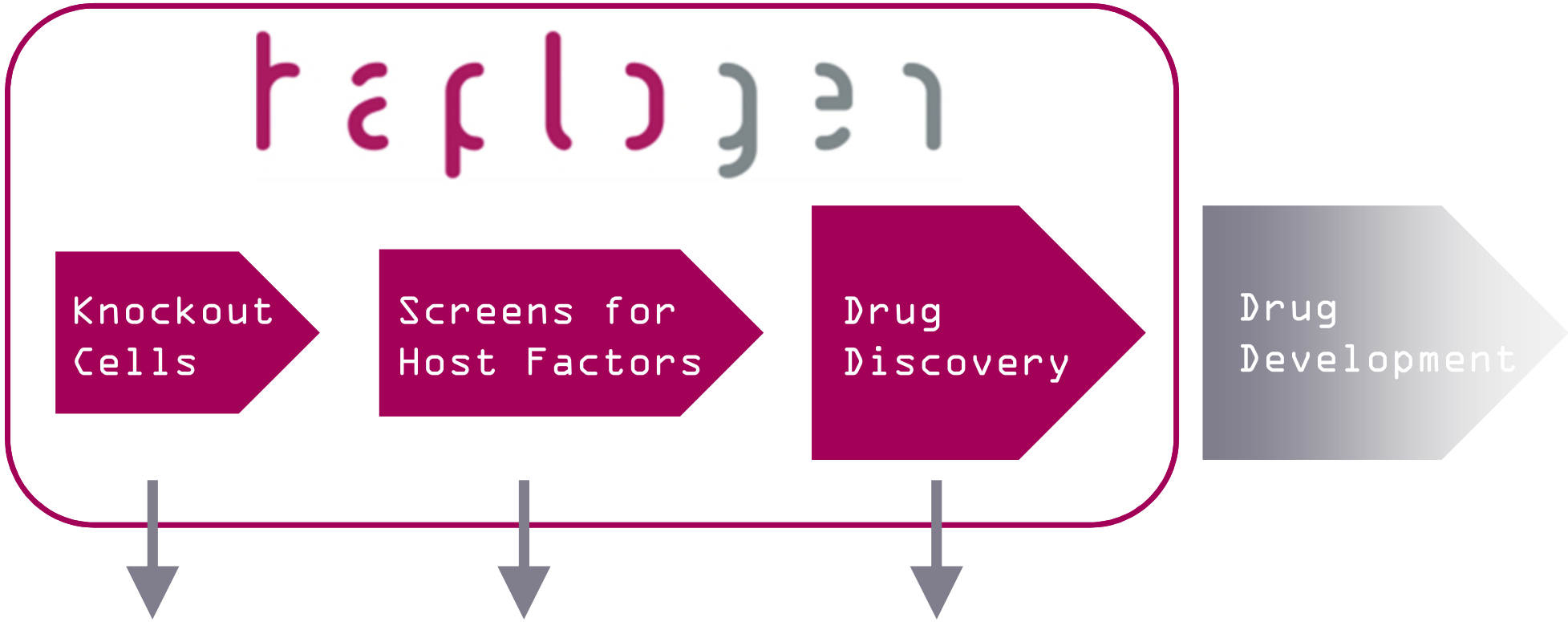


Mutation masked by second copy

Haploid cells

Mutation leads to knockout

Business model



Eine Lizenz zum Klonen

Wie bekommen wir die Rechte nach Österreich?

- Erfindungen müssen patentiert werden
- Die Lizenzen müssen erworben werden

Die ersten Patente

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- Als Wertmarke für Know-how (ein- und aus-lizensieren)
- Als „Betriebslizenz“ (FTO)
- Als Kondensationspunkte um die sich der Firmenwert entwickelt hat (Claims)
- Auch „suboptimale“ Patente können strategisch wertvoll sein

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- Verraten kritische Daten bei Publikation

Technische Machbarkeit und Validierung

„Existenz im Inkubator“

Frühe Tage
was war wichtig für den Erfolg

Public – Private - Partnerschaft – Projekt für eine KO-Klonsammlung

Ce-M-M-
Research Center for Molecular Medicine
of the Austrian Academy of Sciences

2011 **Erste externe Anerkennung unseres Konzeptes**
Förderung im Life Science Call 2011

ZIT ZENTRUM
FÜR INNOVATION
UND TECHNOLOGIE
Die Technologieagentur der Stadt Wien.

Going to „the Hub“ -- „Living on the Edge“

Einzug eigene Räumlichkeiten Campus Vienna Biocenter

AWS seed-financing

Immernoch einzige Aktivitäten technische Entwicklungen

Erste Eigene Patente

Erste eigene Patente für erste aktive Substanzen

Erste Patente zur Technologie an haploiden Zellen

Wichtiges Element für Verhandlungen und um einen Anspruch auf die Assets und Know-How zu dokumentieren!

Entwicklungspartnerschaft zur Therapeutikaentwicklung

Evotec steigt mit Risiko ein – klar komplementäre Expertise

Förderung durch FFG erlaubt Entwicklung mit voller Geschwindigkeit

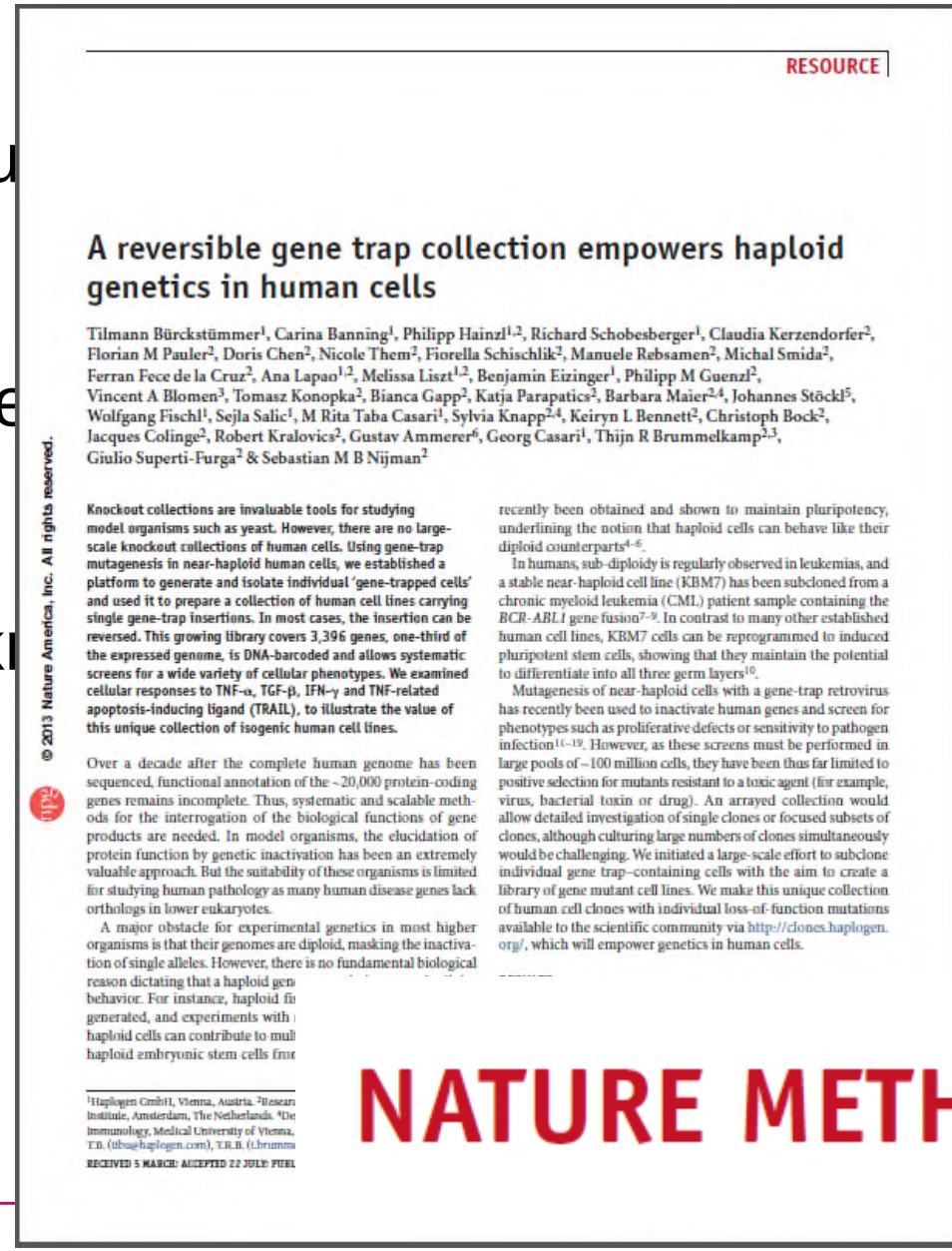
Ein stabiles Produktgeschäft

Produktions und Qu

Vertriebskanal - We

Alleinstellungsmerkr

Markteintritt



RESOURCE

A reversible gene trap collection empowers haploid genetics in human cells

Tilmann Bürckstümmer[1], Carina Banning[1], Philipp Hainzl[1,2], Richard Schobesberger[1], Claudia Kerzendorfer[2], Florian M Pauler[2], Doris Chen[2], Nicole Them[2], Fiorella Schischlik[2], Manuele Rebsamen[2], Michal Smida[2], Ferran Fece de la Cruz[2], Ana Lapao[1,2], Melissa Liszt[1,2], Benjamin Eizinger[1], Philipp M Guenzl[2], Vincent A Blomen[3], Tomasz Konopka[2], Bianca Gapp[2], Katja Parapatics[2], Barbara Maier[2,4], Johannes Stöckl[5], Wolfgang Fischl[1], Sejla Salic[1], M Rita Taba Casari[1], Sylvia Knapp[2,4], Keiryn L Bennett[2], Christoph Bock[2], Jacques Colinge[2], Robert Kralovics[2], Gustav Ammerer[6], Georg Casari[1], Thijn R Brummelkamp[2,3], Giulio Superti-Furga[2] & Sebastian M B Nijman[2]

Knockout collections are invaluable tools for studying model organisms such as yeast. However, there are no large-scale knockout collections of human cells. Using gene-trap mutagenesis in near-haploid human cells, we established a platform to generate and isolate individual 'gene-trapped cells' and used it to prepare a collection of human cell lines carrying single gene-trap insertions. In most cases, the insertion can be reversed. This growing library covers 3,396 genes, one-third of the expressed genome, is DNA-barcoded and allows systematic screens for a wide variety of cellular phenotypes. We examined cellular responses to TNF-α, TGF-β, IFN-γ and TNF-related apoptosis-inducing ligand (TRAIL), to illustrate the value of this unique collection of isogenic human cell lines.

Over a decade after the complete human genome has been sequenced, functional annotation of the ~20,000 protein-coding genes remains incomplete. Thus, systematic and scalable methods for the interrogation of the biological functions of gene products are needed. In model organisms, the elucidation of protein function by genetic inactivation has been an extremely valuable approach. But the suitability of these organisms is limited for studying human pathology as many human disease genes lack orthologs in lower eukaryotes.

A major obstacle for experimental genetics in most higher organisms is that their genomes are diploid, masking the inactivation of single alleles. However, there is no fundamental biological reason dictating that a haploid gen
behavior. For instance, haploid fi
generated, and experiments with
haploid cells can contribute to mul
haploid embryonic stem cells fro

recently been obtained and shown to maintain pluripotency, underlining the notion that haploid cells can behave like their diploid counterparts[4–6].

In humans, sub-diploidy is regularly observed in leukemias, and a stable near-haploid cell line (KBM7) has been subcloned from a chronic myeloid leukemia (CML) patient sample containing the *BCR-ABL1* gene fusion[7–9]. In contrast to many other established human cell lines, KBM7 cells can be reprogrammed to induced pluripotent stem cells, showing that they maintain the potential to differentiate into all three germ layers[10].

Mutagenesis of near-haploid cells with a gene-trap retrovirus has recently been used to inactivate human genes and screen for phenotypes such as proliferative defects or sensitivity to pathogen infection[11–13]. However, as these screens must be performed in large pools of ~100 million cells, they have been thus far limited to positive selection for mutants resistant to a toxic agent (for example, virus, bacterial toxin or drug). An arrayed collection would allow detailed investigation of single clones or focused subsets of clones, although culturing large numbers of clones simultaneously would be challenging. We initiated a large-scale effort to subclone individual gene trap–containing cells with the aim to create a library of gene mutant cell lines. We make this unique collection of human cell clones with individual loss-of-function mutations available to the scientific community via http://clones.haplogen.org/, which will empower genetics in human cells.

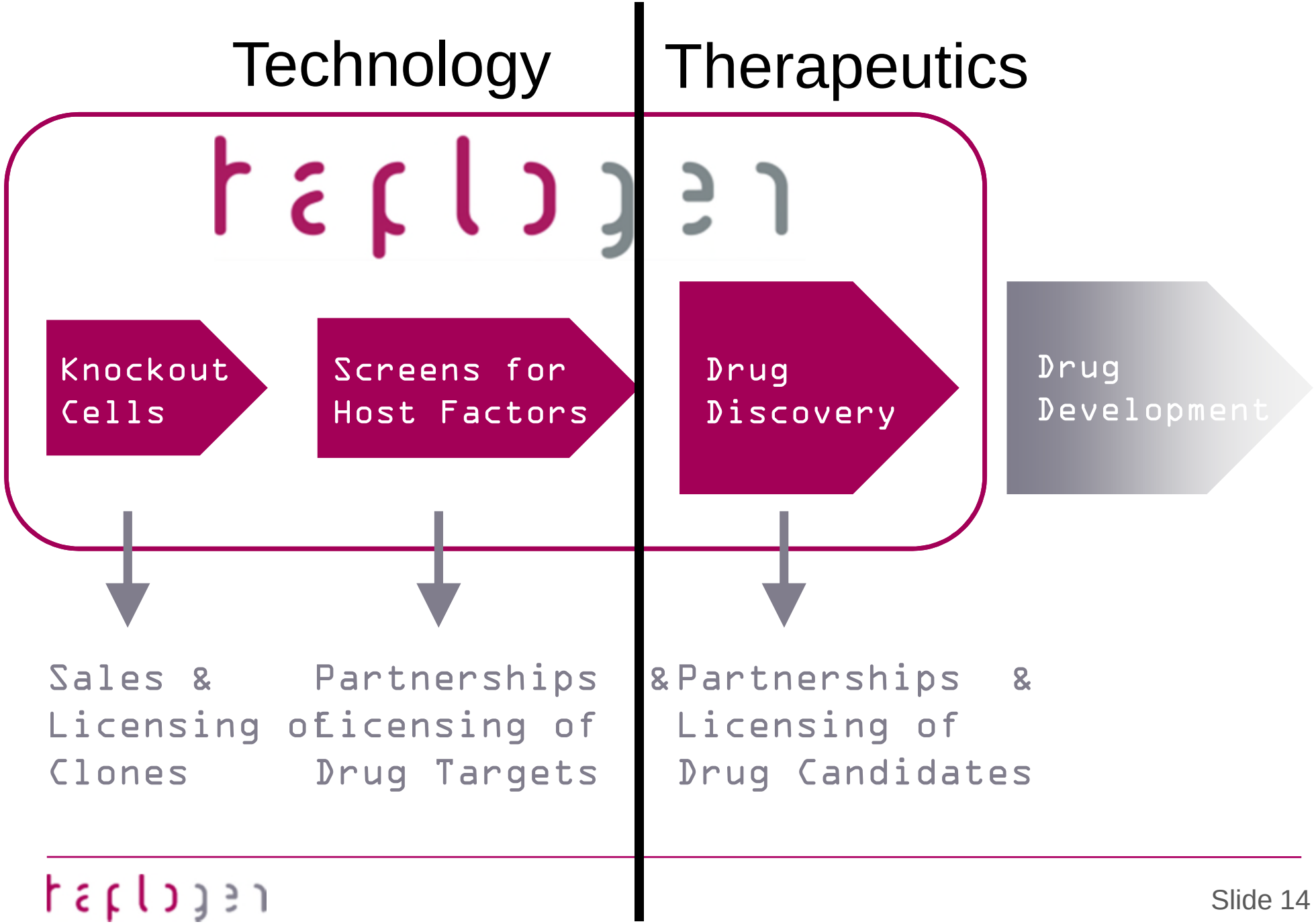
[1]Haplogen GmbH, Vienna, Austria. [2]Resear
Institute, Amsterdam, The Netherlands. [3]De
Immunology, Medical University of Vienna,
T.B. (tbu@haplogen.com), T.R.B. (t.brumm

RECEIVED 5 MARCH; ACCEPTED 22 JULY; PUBL

NATURE METHODS

haplogen

Business model



Ein attraktives Akquisitionsziel

Produkt mit großer, globaler Kundenbasis

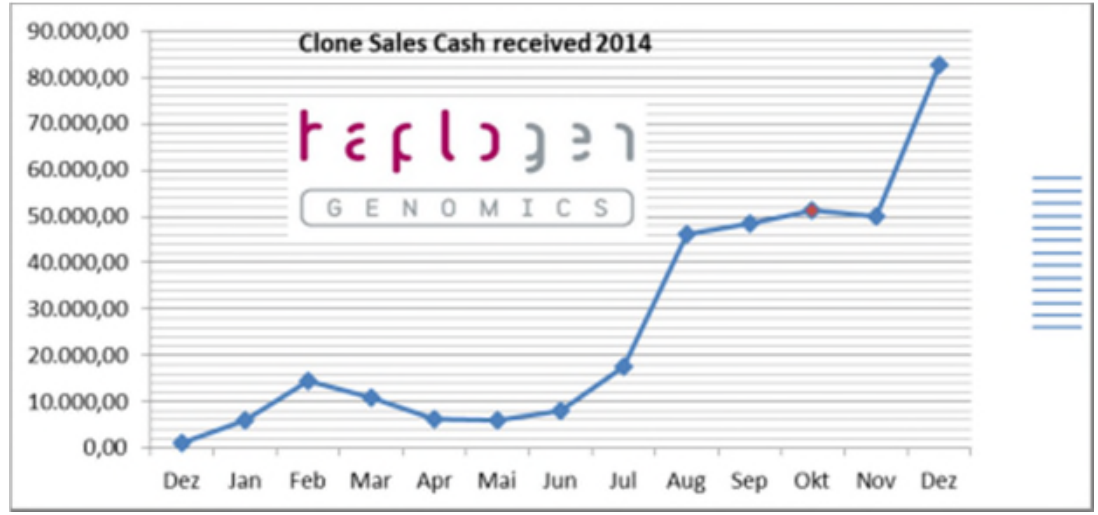
Füllt einen bisher unbedeckten Bedarf

Enormes Umsatzwachstum

Alleinstellung

Vielseitige Einsetzbarkeit

Patente zur Absicherung



Januar 2015: Übernahme der Haplogen Genomics durch Horizon Discovery

Assets: Patente, Kunden, Technologie und Prozesse

Transaktion in Aktien und Bar - 7 Millionen

Meilensteinprämien in Jahr 2 und 3

Standort gestärkt und gesichert –

Wo geht die Reise hin?

- Klares Profil der Haplogen als Anti-infektiva-Firma
- Finanzierung der Entwicklungen für weitere Jahre solide gesichert
- Patente zur Absicherung der Erfindungen und Entdeckungen
- Partnerschaft für klinische Entwicklung angestrebt

- Kapazität für neue Entwicklungsprojekte auf Grundlage der aufgebauten Expertise und Technologie

Acknowledgements

Ce–M–M– Research Center for Molecular Medicine of the Austrian Academy of Sciences

ZIT ZENTRUM FÜR INNOVATION UND TECHNOLOGIE
Die Technologieagentur der Stadt Wien.

aws austria wirtschaftsservice

evotec

ToolGen Genome Engineering

FFG FORSCHUNG WIRKT.

Haplogen Team

Contact us

Haplogen GmbH
Campus Vienna Biocenter 5
1030, Vienna Austria

Phone +43-1-9165522
office@haplogen.com
www.haplogen.com