The Ecstasy of Gold –
Starting your Academic Research and Turning it into a Biotech Startup

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Outline

I. Brief personal intro

II. Industry vs Academia as a Career

III. Developing and commercializing intellectual property within a university setting

Brief Personal Introduction

1976-1980 B.A. Biochemistry/Molecular Biology UC Santa Barbara

Ion chromatography of organic acids in urine

Undergrad research – chromatography of dinoflagelate proteins

1980-1985 Research Assistant 

Purification and characterization of recombinant plasminogen activators

U.S. Patent 5,219,569 Protease Resistant Urokinase (exclusion utility)

1985-1990 Ph.D. Biological Chemistry UC Irvine

Constructed and characterized chimeric serine proteases

1990-1994 Postdoc University of Oregon

Protein crystallography, protein biophysics

1994 FSU Department of Chemistry

2000 Tenured (College of Arts & Sciences)

2005 College of Medicine

2007 Tenured (College of Medicine)

Intellectual property/commercialization efforts:

- **14 issued patents (US and European Union)**

2008 – Co-founded Zign Therapeutics

2012 – Co-founded Trefoil Therapeutics

Industry
vs
Academia
as a career

Imagine a job where everyone spontaneously cheers, high-fives and chants "USA!, USA!, USA!" when a goal is accomplished

- **Genentech *was* like that…**
- **Currently, SpaceX is like that: jubilation with a vertical landing:**

In a company, "*Teamwork*" is the operative word

- **Corporate objectives and goals supersede any one individual's career or advancement**
- **"There is no 'I' in Team"**

Some aspects of a position in Industry to consider:

- Profit sharing/stock options are common (nice!)
- Good benefits (healthcare, retirement, occasionally others – childcare, long-term care, gym membership, reduced cost cafeteria, housing loans, relocation costs, continuing education support, etc.)
- Typical work hours are 9:00-5:00 (evenings and weekends are your own)
  - Consequently, working evenings and weekends can make you stand out
- Competitive salaries and raises (tied to local cost of living)
- The product of the company (a drug, a device, a service, etc.) can have a significant impact upon quality of life of the public (actually useful)
- All employee inventions of are the exclusive property of the company
  - Employee retains no rights of ownership/licensing/royalty
- Legal protection of intellectual property takes precedence over public disclosure, must get legal department approval for:
  - All oral presentations and publications
  - And the legal department is extremely conservative
- Typical layoff notice is 2 weeks (or immediate with severance package)
  - Layoffs can come as a surprise – especially in small companies

For small companies, be aware of the business model/goals of the company founders/CEO/CFO!

- Many small companies have a business goal of being bought out
- Both the risks, and return on investment (ROI), are the greatest when the company is small
  - ROI of >100x for initial investors upon achieving a public offering
    - CEO, CFO, CSO are typically among the initial investors
  - ROI goes down as the company gets larger, more solid
- For a number of CEOs of small companies, this is not their first rodeo
  - They have a clear exit plan 3-5 years away (quit, start another company – maintain that large ROI)
  - Thus, in a small company the major management may depart in 3-5 years; *where does that leave employees*?
- Small companies feel a kindred spirit with employees that have a mature entrepreneurial spirit
  - Employees that have no anxiety about 5 years into the future, and recognize that things can turn south, and *have their own exit plan*

Larger companies are more likely to be structured for long-term employee satisfaction

- Employee retention is a major concern of large companies
  - Turn-over is expensive
  - Large companies are more likely to engage in long-term planning
    - Have income stream to support 5, 10-year business planning
    - May view market share as key aspect of business
- Tend to develop a workforce comprising specific individual expertise rather than employee capability at diverse tasks
  - Can afford to retrain employees
- Have a comparatively large human resource department devoted to employee relations

Academia

Academia is a business, but what exactly is their product?

- Universities strive to develop a reputation for scholastic excellence, and quality of:
  - Education
  - Graduates
  - Faculty
  - Programs and facilities
  - Intellectual property
    - Books, publications, compositions, film, art, etc.
- Academia is less a coherent whole, and more a collection of individuals of repute
- The university hires faculty based upon reputation, or potential to develop or expand upon the University's reputation (in a specific island of excellence)

Some aspects of a position in Academia:

- Salary:
  - Initially nationally competitive; however, low annual raises typically result in salary compression quite quickly (a faculty position is effectively non-movable)
  - University business model provides for a portion of salary, with a requirement for supplementation by grants (10-90%)
- Benefits typically include options for healthcare, long-term care, life insurance, but as specific pre-tax deductions from salary
  - You will have to pay to park at your place of work (geez!)
- Little (if any) recurring funds are provided for research support
  - "Startup" package designed to last ~3 years
  - Assumes that grant support will be obtained by then
- You decide what you will be working on (perceived as the #1 benefit)
  - Your lab is a "Mom & Pop" store (University provides space, lights, water, etc.) - can have a significant impact upon quality of life (general paranoia)
  - Your "team" is your lab group (students, postdocs, technicians, spouse)
  - Once trained and competent, THEY LEAVE! Also, you can't fire students!

Some aspects of a position in Academia (cont.):

- Your goal is to get tenure
  - You cannot continue in a tenure-earning position past year 7
  - Tenure vote is typically in year 6
    - Must have national-level research grant
    - Must have record of publications
    - Evidence of successful teaching
    - Demonstrated service participation
    - Key part of tenure application is outside letters
- Its critical to find out during the job interview what the expectations are for a successful tenure decision
  - It is also key during the job interview to present details of your anticipated first grant application
  - If possible during your postdoc:
    - Collect significant preliminary data
    - Obtain funding that can move with you (this is a tough one, but often the basis for successful job offer)

Some aspects of a position in Academia (cont.):

- All employee inventions of are the exclusive property of the university
  - The university pays all legal costs for patent filing
  - Employee DOES retain rights to licensing/royalty
    - 85% of the first $10,000 in licensing/royalties goes to the inventor(s)
    - After the first $10,000 the university recoups its legal fees, and then subsequent royalty funds are divided:
      - 40% inventor(s)
      - 30% department (typically some kickback to inventor(s))
      - 30% university (typically some kickback to department)
  - If you are going to invent something, *it is substantially more lucrative to do it at a university rather than at a company*
    - The most lucrative situation would be to invent, patent, and license a technology as a private citizen (but then, you have to pay all legal fees)

Bob Holton FSU Chemistry – Taxol semi-synthesis 1989

- **~$200 million in royalties; 40% ($80 million) to Bob Holton (minus legal)**

- **This is Bob**
- **He has reason to smile**

Developing and commercializing intellectual property within a university setting

The process of intellectual property development:

- Invent something (here's the criteria):
  1. Should be patentable (somethings are not patentable but might be copyrighted, e.g. software)
  2. Novel
  3. Non-obvious
  4. Has utility
- Ultimately, a patent examiner at the USPTO will judge the validity of each of these aspects of your patent application

The process of intellectual property development (cont.):

- Submit an invention disclosure to the university office of tech transfer
  - This describes the invention, the potential market, and the inventors
- If FSU is convinced of the utility of the disclosure, they will file a provisional patent application
  - Basically 1-2 page brief description
  - Submission sets the priority date of the application
  - The university has 1 year from the filing date of the provisional to convert to a full application (i.e. to file a full application)

The process of intellectual property development (cont.):

- FSU will hire a lawyer to draft a full patent application
  - Typically pursued ~30 days prior to deadline
  - Lawyer may have a STEM degree, but is unlikely to be familiar with the specific technology
  - It is critical to work with the lawyer to draft a strong application
    - Can take considerable time and effort, but the application will be weak otherwise
    - Costs for this (to FSU and deducted from future royalties) can be >$20,000

The process of intellectual property development (cont.):

- After full conversion submission, USPTO examiner may take 1-2 years (or longer) to review
  - Patents are typically written quite broadly, and the patent examiner will often disallow certain claims in an "Office Action"
  - Disallowed claims are commonly due to being "obvious" (recall the "non-obvious" criteria for patent applications)
  - Also, there can be disallowed claims due to "prior-art" (recall the "novel" criteria for patent applications)
  - Broadly written claims are often considered to consist of more than one claim (and must be broken up)

From bench to bedside: My university research

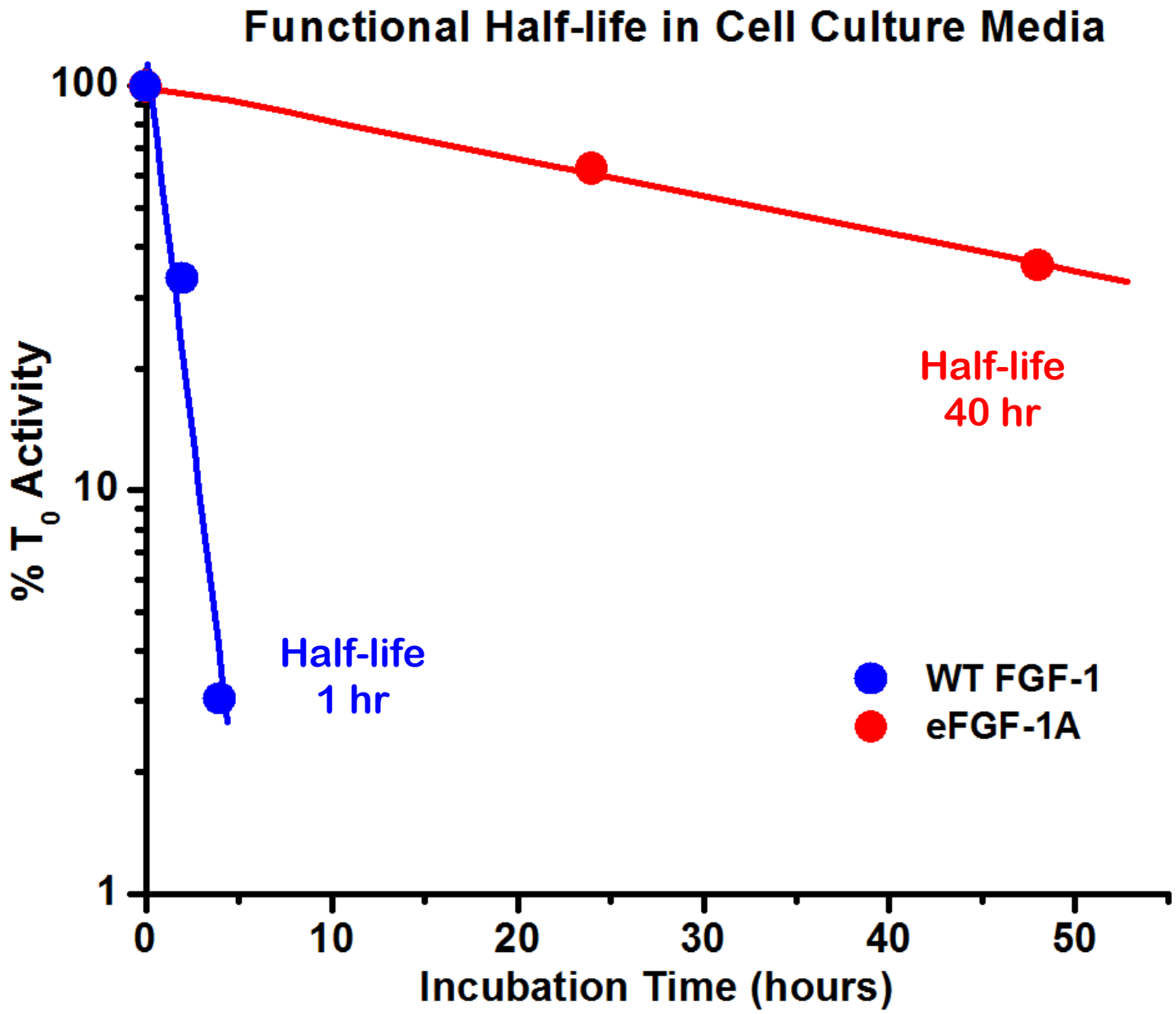
Protein folding, evolution & design

- Did complex protein architecture evolve from simple peptide motifs?
- How is symmetry utilized in protein evolution & design?
- Fibroblast Growth Factor-1 (FGF-1) as the model system in investigating these questions

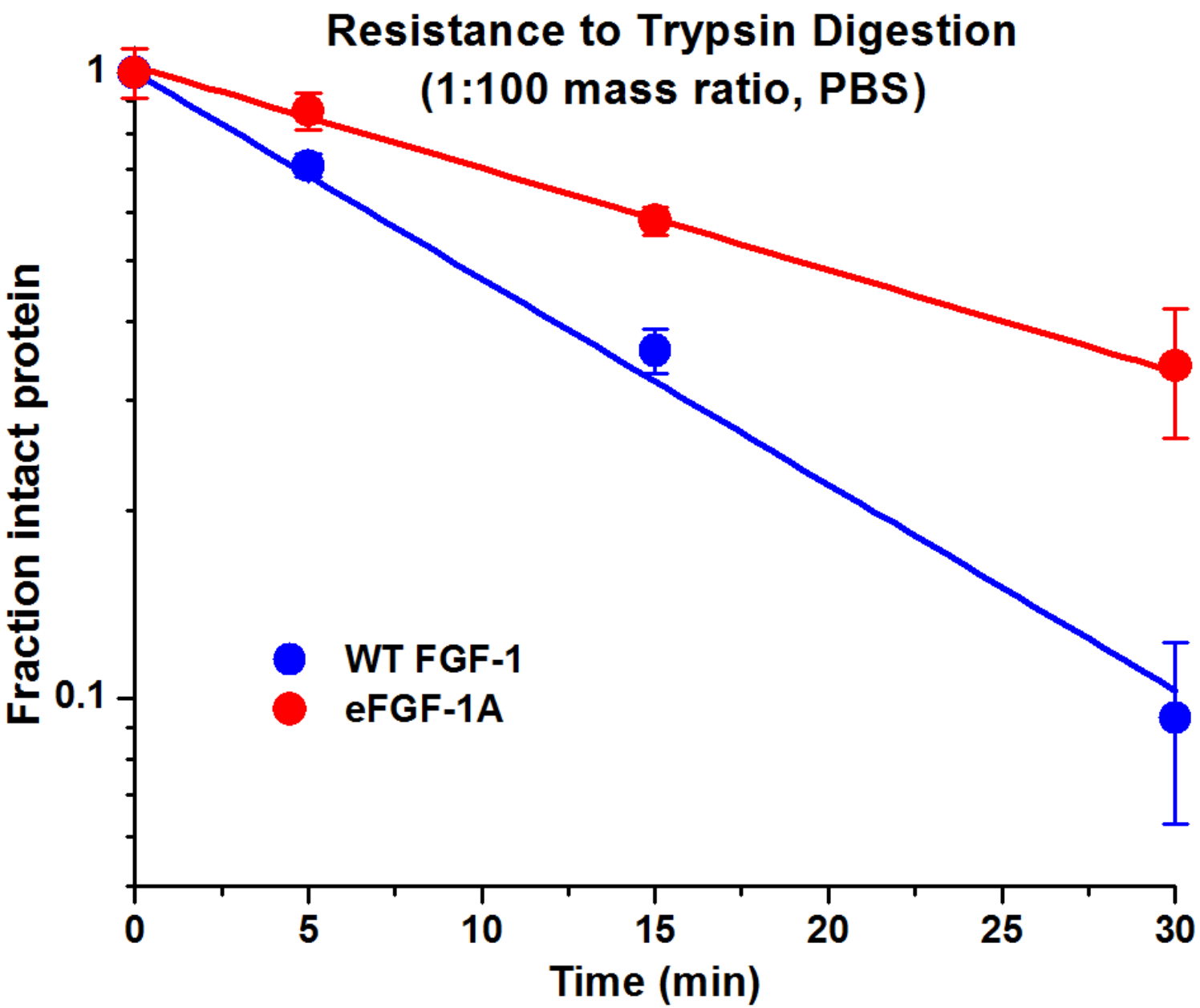
Over the course of this research hundreds of mutant forms of FGF-1 were constructed

- Typically their biophysical properties of folding and stability were characterized, but not functionality (i.e. in vivo properties)
- Upon learning (~2004) that FGF-1 had therapeutic potential, but that this was hampered by poor stability, we decided to also investigate the functional properties of some of our engineered FGF-1 proteins
- eFGF-1A:
  - Increased thermostability
  - Elimination of reactive buried thiols (free cysteines)

Increase in functional half-life in cell culture media:



Resistance to proteolytic digestion in buffered saline:

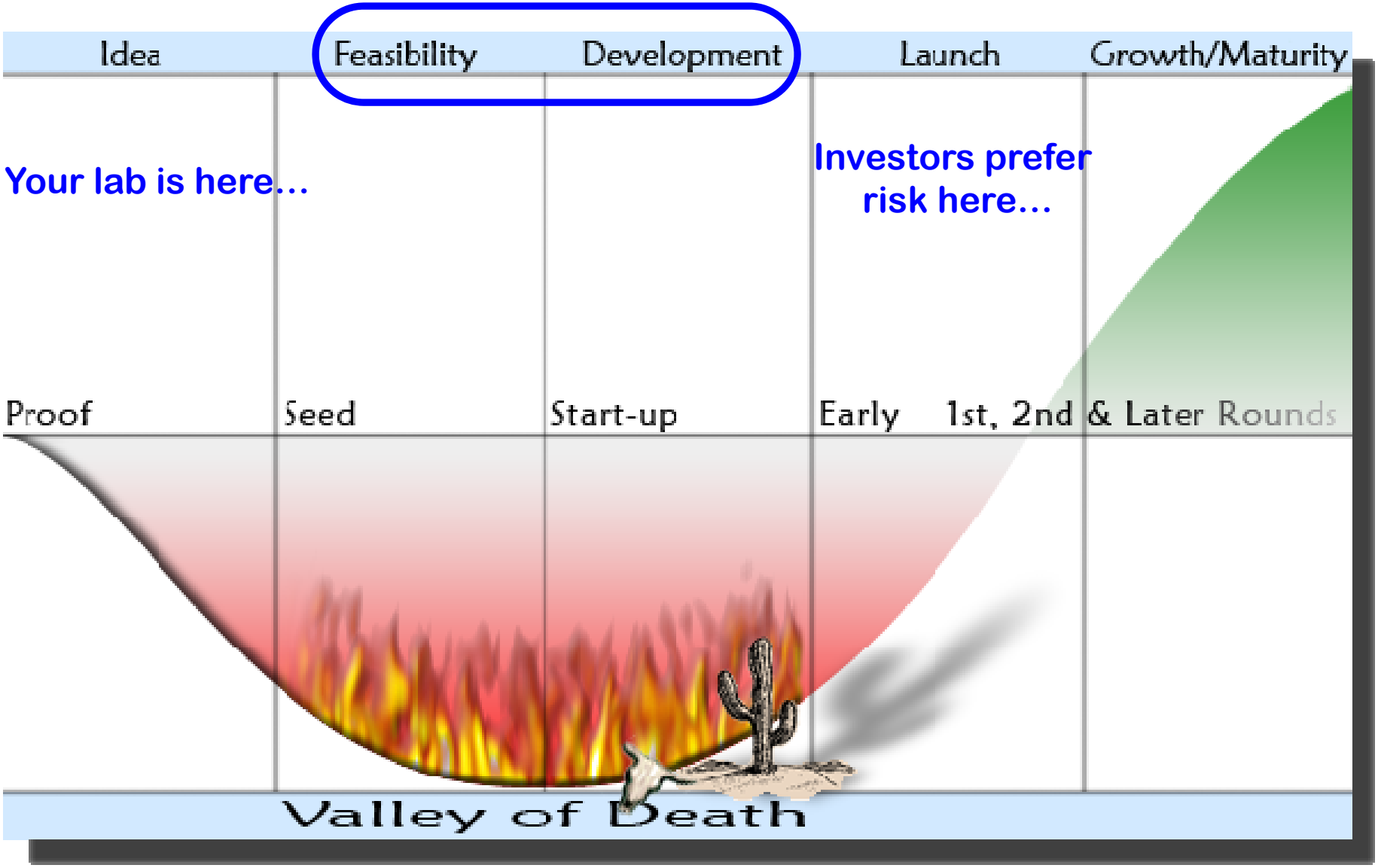


FGF-1 causes many cell types to divide/grow

Potential therapeutic applications in regenerative medicine:

- Acceleration of dermal wound healing (diabetics, elderly)
- Angiogenic therapy in coronary occlusion
- Regeneration of cornea in Fuch's corneal dystrophy
- Regeneration of damaged cornea due to mustard gas exposure (ISIS)
- Novel regulation of blood glucose levels in the diabetic
- However, FGF-1 biophysical properties make it a poor choice as a therapeutic agent (also non-patentable)
    - Stabilizing mutants may solve this problem, and are also protected intellectual property

From bench to bedside – Traversing the Valley of Death…



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Pharmacokinetic Properties of 2nd-Generation Fibroblast Growth Factor-1 Mutants for Therapeutic Application

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1 Department of Biomedical Sciences, Florida State University, Tallahassee, Florida, United States of America, **2** Biomedical Research Laboratory Animal Resources, Florida State University, Tallahassee, Florida, United States of America

Original Research-Basic Science

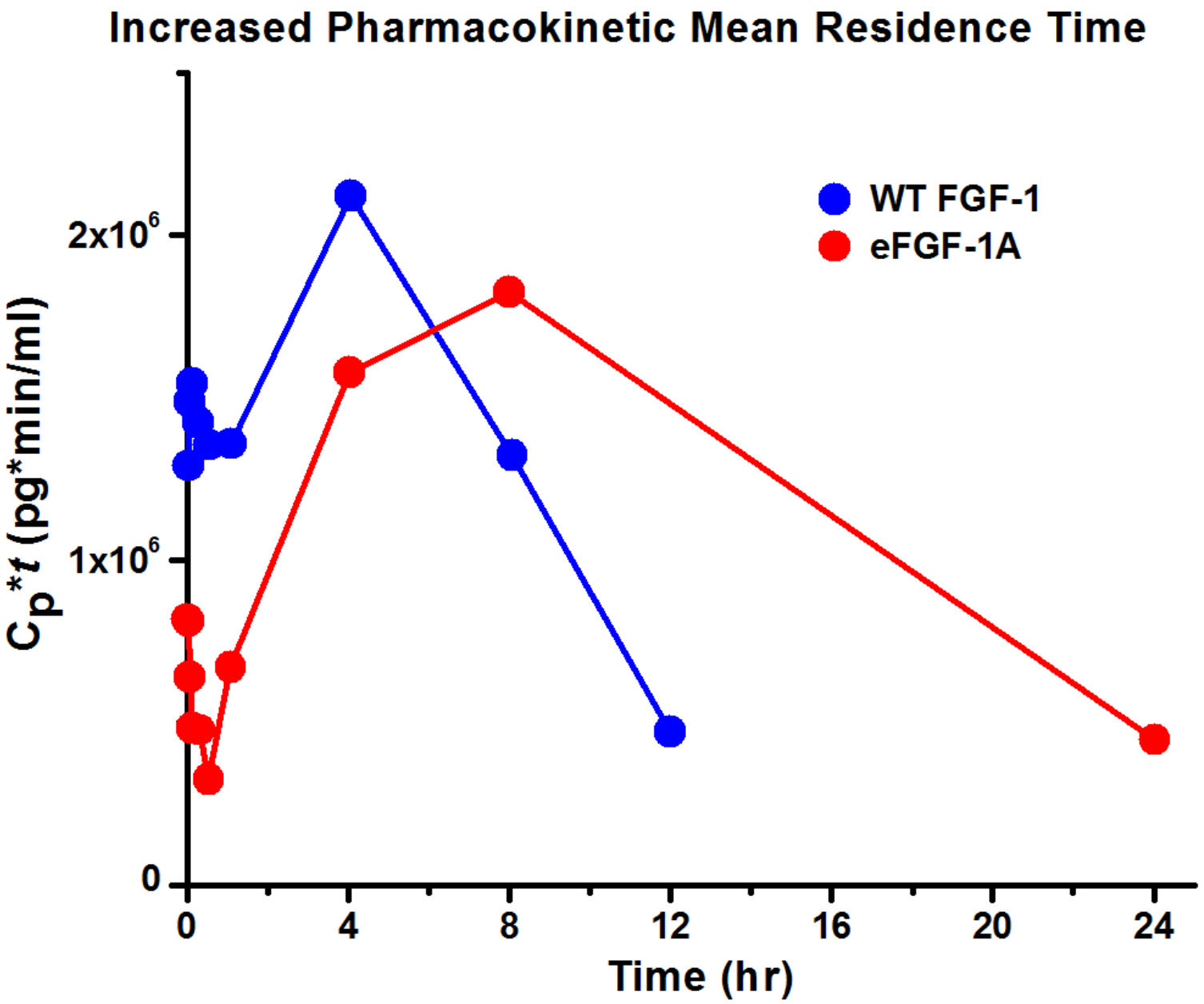
Accelerated healing in NONcNZO10/LtJ type 2 diabetic mice by FGF-1

Sachiko I. Blaber MS, Jose Diaz MD, PhD, Michael Blaber PhD

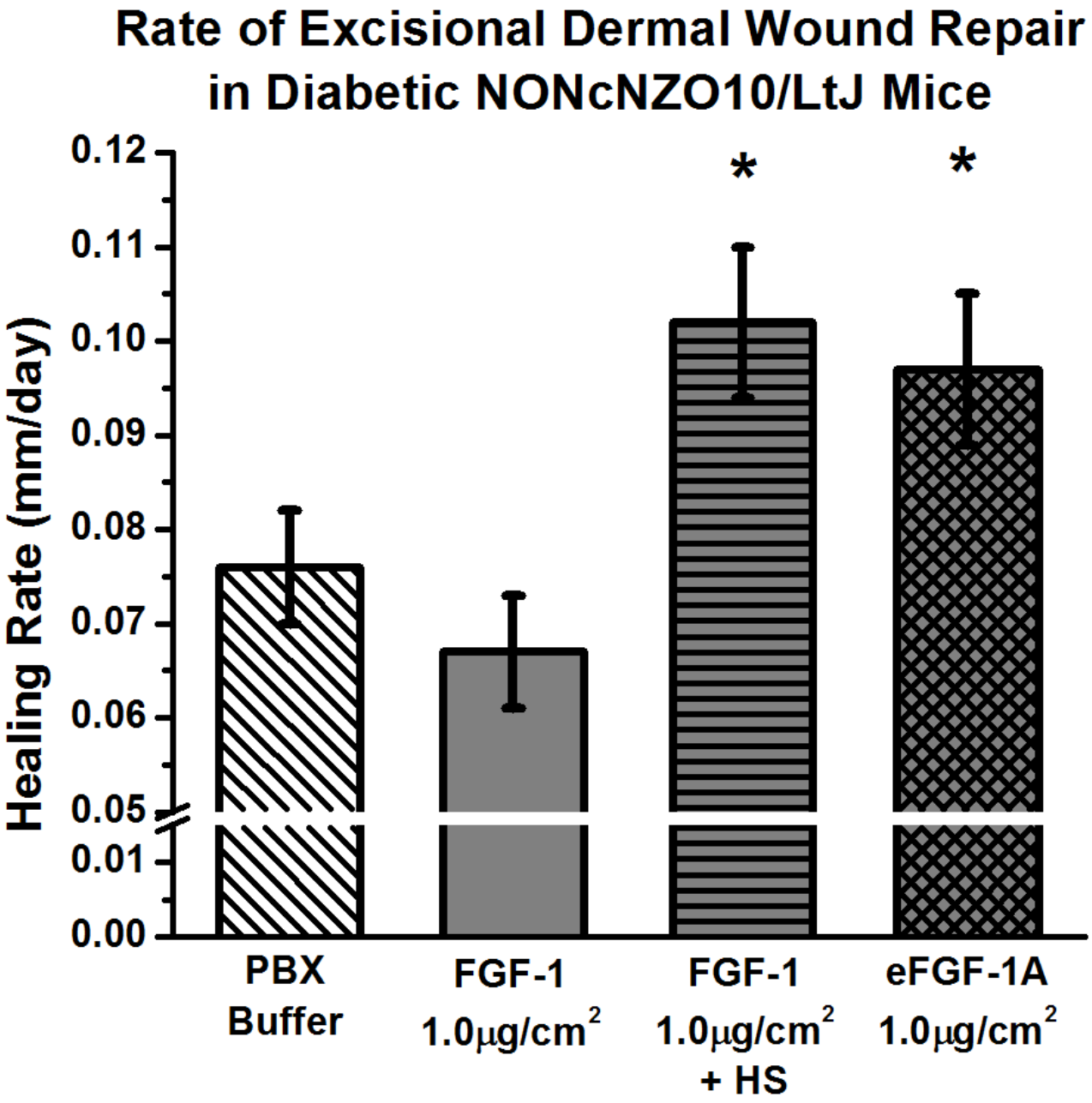
First published: 19 June 2015 Full publication history

Moving from *in vitro* to *in vivo* studies gets expensive quickly…

Enhanced Pharmacokinetic Properties:

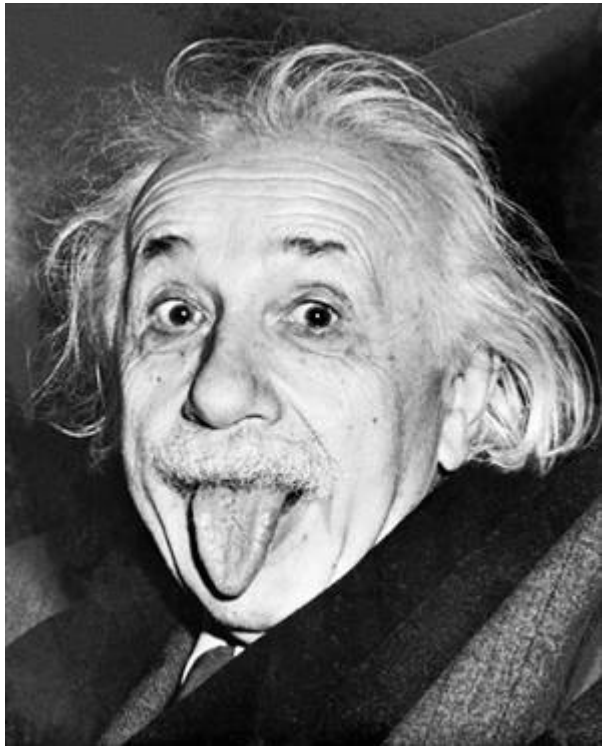


40% enhanced rate of dermal healing in diabetic mice:



A brief history of corporate interest in FGF-1 mutants covered by FSU IP:

- CardioVascular BioTherapeutics (2005)
  - Treating coronary occlusion
- Golden Pine Ventures/Zign Therapeutics (2008)
  - Dermal wound healing
- Phage Pharma (2010)
  - Tympanic (ear drum) repair
- NovoCyte (2011)
  - Burns, autism
- VenaCava Therapeutics (2014)
  - Dermal wound healing
- InnovaTech (2015)
  - Novel bandage technology (dermal wound healing)
- MetaCrine (2015)
  - Blood glucose regulation



"Insanity is doing the same thing over and over again, and expecting a different result"

- Albert Einstein

Trefoil

Management Team

ACT

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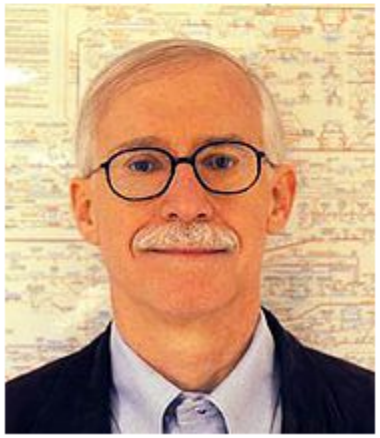
David Eveleth, PhD
Chief Executive Officer

Michael Blaber, PhD
Professor of Biomedical Sciences
College of Medicine
Florida State University
Co-Founder

Ralph Bradshaw, PhD
Chief Scientific Officer



Ken Thomas, PhD
Co-founder/Consultant

Trefoil Therapeutics – A startup biotech company

- **Steps associated with commercialization of FGF-1:**

  1. **Signed 1 year exclusive option to IP (2012)**

     - **Prevents FSU from entering into a license agreement with another party for 1 year**
     - **A short duration option is much cheaper than full licensing**
     - **Provides the company with 1 year to raise the necessary seed capital for a full licensing agreement**
     - **Ties up IP for 1 year – after which, FSU can identify other interested parties if Trefoil fails**
     - **Necessary seed capital funding is "family & friends" (not "series A" as significant proof-of-concept data is needed for series A)**

Trefoil Therapeutics – A startup biotech company cont.

- **2013-2014**
  - **Raised modest funds (<$100K)**
  - **Identified that investor interest was more significant in corneal dystrophy than dermal wound healing**
  - **Established scientific advisory board**
  - **Winner of Early Stage startup competition at 2014 SE BIO forum (mutant FGF-1 for corneal dystrophy)**
  - **Signed licensing agreement with FSU**

Trefoil Therapeutics – A startup biotech company cont.

- **FSU licensing agreement**
  - **Funds up front**
  - **Milestone payments:**
    - **Series A financing**
    - **First-in-human clinical trials**
    - **Drug approval**
  - **Equity (3-4% preferred stock)**
  - **Research support agreement (quarterly payments)**

Trefoil Therapeutics – A startup biotech company cont.

2015-2016: Adding value to the company

- Rented lab space in San Diego, California
- Awarded NIH R21 grant to study FGF-1 mutants to treat eye damage in soldiers due to mustard gas exposure (ISIS)
- Initiated pre-IND discussions with FDA for Fuchs' dystrophy
    - Identified critical studies to enable human trials
- Initiated FDA discussions for Orphan drug status for Fuchs' dystrophy
- Efficacy data generated in-house by Trefoil
- Next step: obtaining series A (first round) financing

QUESTIONS?