FOOD stars — Innovative Food Product Development Cycle: Frame for Stepping Up Research Excellence of FINS

European Commission

Invention Disclosures

Capturing & evaluating IP, patentability, commercial relevance

Sharon Sheahan, Ph.D., Teagasc

Horizon 2020 | European Union funding for Research & Innovation
Grant Agreement number: 692276 — FOODstars | H2020-TWINN-2015

Invention Disclosures – Why?

- Societal benefit – making our world and people's lives better
- €€€ investment of our money
- National policy
- Institutional policy
- Funding requirements
- Revenue
- IMPACT – measuring project outputs, patent, product, industry, publications, recognition, track record, career opportunities

Benchmarking

Research outputs	per €100 million research expenditure
Invention Disclosures	60
Patents	25
Licences	20
Spinouts	4

Invention Disclosure Form - IDF

- recording of inventions, discoveries, materials, processes, databases, formulations, know-how, trade secrets, software
- technologies with commercial applications/value, project outputs, impact
- a complete, *enabling* description so that someone of ordinary skill in the art could reproduce and practice the invention; including deposit of bacterial strains to culture collection repository

Anatomy of an IDF - Key Sections

- Background to the technology area, what is already known – 'prior art'
- Technical description: in layman's terms, what the invention is and how it works, what problem does the invention solve
- Novelty and advantages over existing technologies:

- How is the invention different to existing solutions

- What advantage does the invention have over existing similar technologies

Anatomy of an IDF - Key Sections

- stage of development: idea, proof of concept, prototype model, demonstrated practically, validated, animal/human studies
- commercial applications
- relevant, interested companies

Disclosures

- disclosing your invention to the public in any way can be ‘novelty-destroying’ and prohibit patent filing:
- abstract, poster, paper, thesis, lecture/seminar, meetings, discussions, collaborators, media, internet
- always check with your TTO in advance
- confidentiality Agreements facilitate discussions and exchange of information

Materials

- any use of materials (clinical samples, food samples, strains, compounds) databases, equipment, software, information from external sources
- make no assumptions regarding permission to use or ownership of results/outputs
- MTA - agreement governing use of the materials for a specific purpose
- Informed consent must be obtained for use of clinical samples

Inventors

- must make an intellectual contribution to the invention, rather than just carrying out technical instructions
- must provide written description of contribution
- often groups of researchers and collaborators
- % contribution to the invention to be agreed among inventors, otherwise assumed to be equal
- revenue sharing among Inventors

Inventive Contribution

- invention is defined as conception of an inventive idea coupled with a reduction to practice to create a working example of that idea
- problem-solving and improvements to original concept
- not routine supervision or passive implementation
- not obvious
- a legal test, unlike ‘courtesy’ authorship on a manuscript
- correct inventorship, to avoid invalidating patent

Funding

- Include all sources of funding used: grants, Industry
- Terms and conditions of funding: fulfill IP obligations to funding agencies, companies

Ownership

- Based on inventive contribution and funding terms
- Often joint ownership with collaborators
- Collaboration Agreement terms
- Joint Ownership Management Agreement upon creation of IP

IDF Evaluation

- Technology
- Materials
- Disclosures
- Inventors
- Funding

Patentability Evaluation

- To qualify for patent protection, an invention must be:

- *novel*: must not have been disclosed to public, patented nor published by anyone else previously

- *inventive*: must involve an inventive step not obvious to someone skilled in the relevant field*

- *useful*: must be capable of industrial application

* a hypothetical, unimaginitive person, considered to be in possession of common general knowledge in the field concerned, and to have access to all relevant prior art documents

Prior Art Searches

- Anything made available to the public by written or oral disclosure or use, prior to filing patent
- Literature and patent databases
- Keywords & combinations

Patentability Opinion

- Engage with patent attorney
- Patent attorney engages with Inventors
- Professional Patentability Opinion obtained to inform decision-making

Commercial Evaluation

- Market validation: gap, size, trends, barriers
- How will the invention address the gap
- Competitors
- Competitive advantage
- engagement with potential customers/licensees/end-users
- Commercial Plan outlined

Possible Evaluation outcomes

- Patent filing - if novelty, inventiveness, commercial potential and commercial plan established
- Put on ‘hold’ and await further data
- Apply for funding to develop further
- Marketing to validate commercial interest
- Balance publication needs of researcher

Examples of Teagasc IDFs in Food Space

- Probiotic/Bacteriophage/bacteriocin antimicrobials:

  C. difficile, Listeria, Salmonella, MRSA, Pseudomonas, mastitis
- Health-promoting Probiotics: CLA, GABA, EPS-producers
- Prebiotic fibres: healthy microbiota, gut health
- Food diagnostics: *B. cereus,* Sulphite-reducing clostridia, Cheese Pinking
- Protein extraction: fish, meat waste
- Encapsulation: probiotics, vitamins, sensitive components
- Cheese-making processes: reduced-fat/salt, flavour, stability
- Dairy processing: Wheyless Cheese, Toddler Milk

IDF Case Study 1: Thuricin

Thuricin - an antimicrobial for specifically targeting *Clostridium difficile*

The Problem: *Clostridium difficile*

- Major gastrointestinal infectious agent, 'Superbug'
- Hospital-acquired infection, *C. difficile* infection (CDI)
- Causes 15-25% of antibiotic-associated diarrhoea
- Causes >90% pseudomembranous colitis
- Mortality rate ~20%
- Recurrence rates 10-50%
- Antibiotics standard treatment

Clostridium difficile Infection (CDI)

World Health Organization

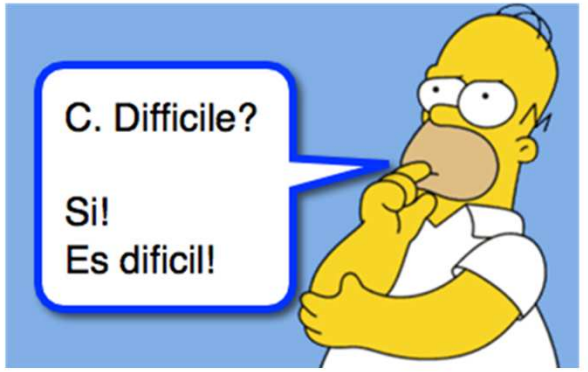
a centre | Publications | Countries | Programmes | Governance

Media centre

The world is running out of antibiotics, WHO report confirms

News release

20 SEPTEMBER 2017 | GENEVA - A report, *Antibacterial agents in clinical development – an analysis of the antibacterial clinical development pipeline, including tuberculosis*, launched today by WHO shows a serious lack of new antibiotics under development to combat the growing threat of antimicrobial resistance.



SEARCH | NEWSLETTERS | CROSSWORD | NOTICES

THE IRISH TIMES

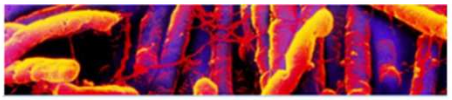
NEWS | SPORT | BUSINESS | OPINION | LIFE & STYLE | CULTURE

Health | Budget 2018 | Ireland | World | Politics | Crime & Law | Social Affairs | Educ

C.diff more common than MRSA but public not aware

Tue, Mar 4, 2014, 01:00

Michelle McDonagh



THE IRISH TIMES

Fri, Oct 6

NEWS | SPORT | BUSINESS | OPINION | LIFE & STYLE | CULTU

Budget 2018 | Ireland | World | Politics | Crime & Law | Social Affairs | Health

HSE's Ennis probe finds 15 died with superbug

Thu, Apr 10, 2008, 01:00

PAT FLYNN

CURRENT THERAPY

The major predisposing factor for CDI is use of broad spectrum antibiotics

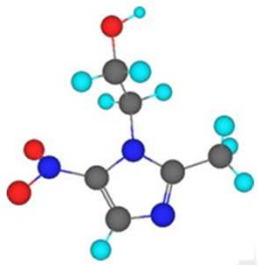
Broad spectrum antibiotics

↓

Disruption of gut microbiota

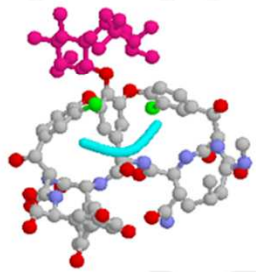
↓

C. difficile proliferates



Current treatment

Vancomycin
Metronidazole



10-50% recurrence rate

Aim to find a solution that may:
- reduce antibiotic use
- aid microbiota recovery
- reduce *C. difficile* shedding
- reduce recurrence

Technical Description: the Solution

- **Antimicrobial with high specificity for *C. difficile* and low collateral damage**
- Screening: Human fecal samples plated, overlaid with *C. difficile*
- 30,000 colonies showed zones of inhibition; just one had large zone
- Strain identification: Bacillus Thuringiensis
- Bacteriocin identification: Thuricin antimicrobial, 2-peptide bacteriocin (Trnα and Trnβ)
- potent activity, heat and pH stable, protease-sensitive

Novelty and advantages over existing technologies

- good efficacy, comparable to competitor vancomycin
- high specificity, very narrow spectrum
- little collateral damage to beneficial microbiota eg. LAB, Bifs, & much less than competitors
- unusual 2-component bacteriocin

***Novel, effective, specific therapeutic for CDI in peptide, probiotic or spore form**

Disclosures

- Conference abstract, poster, presentation
- Source, name of strain and bacteriocin omitted
- ‘non-enabling disclosure’ of the invention confirmed

Materials & Ownership

- Consent obtained for use of human fecal samples
- *B. thuringiensis* strain and bacteriocin isolated by owned by Teagasc

Inventive Contribution & Funding

- 3 Inventors: Teagasc and University College Cork, jointly-owned, equal contribution
- Funding: Research Centre Grant
- Collaboration Agreement: Industry first option to license

Stage of Development

- Peptides characterised
- Fecal fermentations showing efficacy
- Animal studies showing efficacy

Commercial application

- Method of treatment of *C. difficile* infection

IDF Evaluation - Patentability

- Novelty ✓
- patent, literature, genome databases searched
- narrow spectrum, very low activity against Gram +ve, no Gram –ve activity, unlike other *B. thuringiensis* bacteriocins
- novel bacteriocin structure
- Inventive step ✓
- 30,000 colonies screened, spore-forming gut bacteria not obvious source, unexpected lack of Gram +ve activity
- Utility ✓ treatment of *C. difficile* infection

IDF Evaluation - Commercial

- Commercial Case ✓
- significant market
- potential Licensee on board

Area	Period	No. cases	Cost to economy (per annum)
Ireland	2015	1,943	€ 21.25 million
UK	2015/2016 (12 mo)	14,139	£ 141.5 million
US	2015	293,300	US$ 6.3 billion

IDF Evaluation Outcome – File Patent

- Patent filed in European Patent Office, to get Search Report
- Strain deposited in NCIMB for enabling disclosure
- IP assignments obtained from Inventors

- Patent Claims:

- A strain of bacteria, Bacillus Thuringiensis, and similar
- A bacteriocin produced by the strain effective against *C. difficile*
- Formulations: probiotic, peptide, dietary supplement, pharmaceutical composition, encapsulated forms

Commercialisation – Licence no. 1

- Issued Option to License to Industry Partner
- Industry Partner exercised their Option
- Licence negotiated: exclusive, worldwide rights
- Licence fees: upfront, annual maintenance, milestones, royalties, patent costs

Commercialisation Plan - Milestones

- Production of the peptides
- Formulation of Thuricin therapeutic
- File IND (investigational new drug)
- Phase I, II, III clinical trials
- Sales – predicted revenue $40m annually

Technical limitations

- Insufficient peptide production through fermentation and purification for clinical trials
- Synthetic production expensive
- Commercial decision taken by Company to terminate licence

Commercialisation – Licence no. 2

- Technical limitations:

- peptide instability due to pH & enzyme sensitive in upper GI tract
- pharma production more expensive than competitors
- lengthy development plan: time & €€€
- Company terminated the licence

Lessons

- Just because it works in the lab and is patentable doesn't mean it is commercially viable
- Scale-up and production problems in the real world
- Desirable solution but considered too expensive to bring to the clinic

Benefits

- High impact research and publications
- Attracted high profile industry and collaborators
- Patent costs recouped

IDF Case Study 2: CLA-producing strain

Modulation of tissue fatty acid composition by human gut bacteria producing CLA

(*CLA, conjugated linoleic acid)

The Problem

- Inflammation involved in disease: immune, digestive, cancer, obesity

Technical Description: the Solution

- **Bacterial strains that increase CLA levels *in vivo* and reduce inflammation**
- Known that CLA has anti-inflammatory effects
- Identified 3 bacterial strains that increase CLA levels *in vivo*
- Mechanism is by converting polyunsaturated fatty acids to CLA
- Reduced inflammatory cytokines and inflammation

Materials – issue identified

- Best CLA-producing strain from NCIMB Culture Collection
- Not owned by Teagasc
- Deposited in NCIMB in 1950's
- Researcher deceased, not possible to seek transfer of ownership
- Publicly available to competitors
- Patent claim to the strain not possible, 'use' claim only

IDF Evaluation

- Novelty ✓
- Probiotic strains increased CLA levels *in vivo*
- *In vivo* incorporation of CLA not previously demonstrated
- Continuous low level production of CLA desirable
- Inventive step ✓
- Only certain CLA-producing strains could increase CLA levels *in vivo*, not obvious which
- Utility ✓
- treatment of inflammatory disease

IDF Evaluation - Commercial

- Commercial Case ✓

- significant market
- potential Licensee on board
- discussed strain ownership issue with Licensee

IDF Evaluation Outcome - Patent

- Patent filed in European Patent Office, to get Search Report
- 2 out of the 3 Bifidobacterial strains deposited in NCIMB for enabling disclosure
- IP assignments obtained from Inventors

- Patent Claims:

- Use of a CLA-producing strain of bacteria for the *in vivo* conversion of dietary polyunstaurated acids to CLA in the gut
- Use of a CLA-producing strain to alter the fatty acid composition of internal organs of the body
- Use of a CLA-producing strain for the treatment of inflammatory diseases
- Probiotic compositions including foodstuffs such as yoghurt, cheese

Commercialisation - Licence

- Issued Option to License to Industry Partner
- Industry Partner exercised their Option
- Licence negotiated: exclusive, worldwide rights
- Field: Food, Medical Foods, Infant Formula, Animal Feed
- Licence fees: upfront, annual maintenance, milestones, royalties, patent costs

Commercialisation Plan - Milestones

- Redeposit and rename strain to facilitate control and branding
- Ingredient formulation
- Pre-clinical testing
- Food intervention trials
- Sales

Lessons

- Check the source of all materials introduced and used in projects
- Establish ownership at the outset to inform decision-making early
- Patent claims aren't everything – strong brand, trademark, first to market, esp. for probiotics/food

Thank you for your attention

Questions?