Invention Disclosures

Capturing & evaluating IP, patentability, commercial relevance

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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

<table>
<thead>
<tr>
<th>Research outputs</th>
<th>per €100 million research expenditure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invention Disclosures</td>
<td>60</td>
</tr>
<tr>
<td>Patents</td>
<td>25</td>
</tr>
<tr>
<td>Licences</td>
<td>20</td>
</tr>
<tr>
<td>Spinouts</td>
<td>4</td>
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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: 
  \textit{C. difficile}, Listeria, Salmonella, MRSA, Pseudomonas, mastitis
- Health-promoting Probiotics: CLA, GABA, EPS-producers
- Prebiotic fibres: healthy microbiota, gut health
- Food diagnostics: \textit{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)

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.

THE IRISH TIMES
Fri, Oct 6, 2017

C. difficile more common than MRSA but public not aware
© Thu, Apr 18, 2016, 01:00
Michelle McGlinchy

HSE's Ennis probe finds 15 died with superbug
© Thu, Apr 18, 2016, 01:00
PAT FLYNN

Innovative Food Product Development Cycle: Frame for Stepping Up Research Excellence of FINS
The major predisposing factor for CDI is the use of broad spectrum antibiotics. Current treatment options include Vancomycin and Metronidazole, which can reduce the recurrence rate to 10-50%. The aim to find a solution that may include:
- Reduce antibiotic use
- Aid microbiota recovery
- Reduce C. difficile shedding
- Reduce recurrence

Current therapy includes broad spectrum antibiotics, disruption of gut microbiota, and C. difficile proliferates.
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

<table>
<thead>
<tr>
<th>Area</th>
<th>Period</th>
<th>No. cases</th>
<th>Cost to economy (per annum)</th>
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<tbody>
<tr>
<td>Ireland</td>
<td>2015</td>
<td>1,943</td>
<td>€ 21.25 million</td>
</tr>
<tr>
<td>UK</td>
<td>2015/2016 (12 mo)</td>
<td>14,139</td>
<td>£ 141.5 million</td>
</tr>
<tr>
<td>US</td>
<td>2015</td>
<td>293,300</td>
<td>US$ 6.3 billion</td>
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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 \textit{in vivo} conversion of dietary polyunsaturated 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?