An Roinn Talmhaíochta,
Bia agus Mara
Department of Agriculture,
Food and the Marine

15F604 - Thermal or membrane processing for infant formula

Final Report

This project was funded under the Department of Agriculture, Food and the Marine Competitive Funding Programme.

SUMMARY

This project produced, at pilot plant scale, Infant Milk Formula (IMF) by cascade membrane filtration. Product safety of this IMF is comparable to formula produced by standard high temperature processing. However, it contains significantly more native whey protein, resembling that of breast milk. The kinetics of protein digestion in the in vitro and in vivo gut demonstrated that this IMF is faster to digest than IMF produced by high temperature. Although the majority of peptides that cross the in vitro gut barrier post digestion, are similar for both processes, there were some unique peptides identified for cascade membrane filtered IMF. These bioavailable peptides had additional health benefits to fat and muscle cells in vitro. A 28-day dietary intervention study in young piglets, demonstrated that processing type did not influence growth trajectories or food conversion efficiency.

TOMI delivered a nutritional enhanced IMF which will be off benefit to those babies fed IMF or IMF follow-on products in the future. The digestion, bio accessibility and bioavailability research capacity built in TOMI can offer a service to food manufacturers to test efficacy of nutrients in food matrices as the consumer continues to look for alternatives to meat and milk. The scientific highlights included the development of a semi dynamic model of the infant gut, and this project was the first in the world to report the development of an infant gut barrier in vitro.

KEYWORDS

Infant formula, processing, protein digestion

ACRONYM	TOMI
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COLLABORATORS, INSTITUTION	Dr Michael Callanan, Cork Institute of Technology.
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Section 1 - Research Approach & Results

Start Date

01 March 2017

End Date

30 November 2021

Research Programme

Food Institutional Research Measure

TRL Scale

TRL 5: Technology validated in relevant environment

NRPE Priority area

Food for Health

Total DAFM Award

€590,964.00

Total Project Expenditure

€539,658.09

Rationale for undertaking the Research

Infant formula is consumed by the most sensitive of populations, infants and young children under 36 months of age. While conventional thermal processing has documented nutritional and safety benefits, it also has deleterious effects on food structure, bioactives, proteins, oxidation of fatty acids and causes the formation of undesirable Maillard reaction products. Ultra-high temperature processing of milk proteins will destroy native structure of soluble fractions, affecting proteolysis, disintegration in gastro-intestinal tract and rate of digestion. Breast milk does not undergo any processing and therefore the native structure of the protein is maintained. From a health perspective, the incidence of necrotizing enterocolitis in formula-fed preterm babies is higher than in breast fed babies, so the continued development of next generation IMF that more closely resembles breast milk may help to reduce the rates of this illness.

TOMI aimed to investigate if cascade membrane filtration was a safe, viable alternative technology in the pilot plant to Ultra high temperature processing. Whether or not this membrane filtered IMF product had increased native whey and whether this impacted on digestion or indeed bioavailability was investigated both in vitro and in vivo, using state of the art in vitro models and using a dietary intervention trial with piglets.

Methodology

TOMI exploited Teagasc's knowledge base on membrane separation to deliver IMF from deconstruction of milk and subsequent recombination into a nutritionally complete IMF. The microbial safety of the membrane separated IMF produced at pilot plant scale was thoroughly evaluated. From a chemical safety perspective, levels of carboxymethyl-lysine, a key marker of Maillard reaction, was quantified by Liquid Chromatography /Mass Spec. Compositional analysis and structure of dairy protein in the formulation was analysed by Kjeldahl, size exclusion chromatography and reverse phase High Performance Liquid Chromatography. INFOGEST static and semi dynamic in vitro models of gastrointestinal digestion in the infant gut were employed to track protein digestion in the

gastric and intestinal phases. We also employed the piglet, as an animal model of the infant gut, to determine protein digestion and growth parameters in vivo. Which dairy peptides were capable of crossing the gut barrier were investigated by using polarised Caco2 monolayers. Bioactivities of bioavailable peptides and pig blood was assessed by growth and metabolic activities of fat (3T3-L1) and muscle (C2C12) cells in vitro. In addition, we developed an in vitro model of the new-born gut barrier by treating Caco2 monolayers with sodium butyrate.

Project Results

There were four main deliverables during the lifetime of the TOMI project:

1. 100kg Infant milk formula suitable for babies 0-6 months old was produced by cascade membrane filtration.
2. 100kg infant formula suitable for babies 6-12 months produced by cascade membrane filtration.
3. An in vitro infant model of the gut barrier was developed.
4. A semi dynamic model of infant gastrointestinal digestion was developed.

TOMI delivered on all of its objectives by producing a nutritional enhanced IMF using cascade membrane filtration (CMF-IMF). TOMI demonstrated that this alternative process can produce an IMF that is microbial safe but has less undesirable products of thermal treatment, when consumed, compared to the current high heat processing (HT-IMF). TOMI fully characterized the chemical, physicochemical and micro-structure of this next generation IMF. This revealed significantly more native whey (59.9%) compared to HT-IMF (4.5% native whey). Therefore CMF-IMF more closely resembles breast milk (100% native whey). The project then tracked protein digestion in the upper gut using both 'state of the art' INFOGEST in vitro models and using a 28-day dietary IMF intervention in piglets. Protein digestion in the gut was influenced by processing method with significantly higher water-soluble peptides present in the stomach in vitro and in vivo. There was a significantly higher degree of protein hydrolysis in the stomach and duodenum of CMF-IMF fed piglets compared to their HTIMF fed counterparts. This resulted in a peak increase of free amino acids in the jejunum. The abundance of peptides within certain size ranges in the duodenum, jejunum and ileum was dependent on processing. We can conclude that CMF-IMF is faster to digest that HT-IMF. Although the majority of peptides that cross the in vitro gut barrier are similar for both IMFs, there were some unique peptides identified for CMF-IMF. In vitro, these bioavailable peptides had additional health benefits to muscle cells and fat cells. In addition, the in vitro gut barrier was also healthier with increased tight junction proteins when treated with CMF-IMF compared to HT-IMF.

In the dietary intervention trial, overall growth and feed intake parameters were unaffected by IMF processing albeit some transitory differences were observed. We can therefore conclude that CMF-IMF more closely resembles breast milk, is safe for human consumption, is easier to digest than HT-IMF, satisfies normal physical growth and may have additional health benefits.

Section 2 - Research Outputs

TOMI produced a next generation Infant Milk Formula (IMF) 100kg without compromising safety, that more closely resembles breast milk and is easier to digest for the infant, than IMF produced by traditional high heat.

The benefits to Industry are:
This offers industry a choice to lower heat during IMF processing without compromising on safety. The digestion, bio accessibility and bioavailability research capacity built in TOMI can offer a service to food manufacturers to test efficacy of nutrients especially proteins in food matrices. The interest and relevance to industry is evidenced by industry funding of follow-on projects to TOMI PIs. Ireland's economic development was supported by TOMI, through the training of 4 skilful, well-educated scientists and hosting 2 PhD students from overseas.

The benefit to the consumers is:
This next generation IMF with its gentler processing will be off benefit to those babies fed IMF or IMF follow-on products in the future. In addition, the in vitro infant gut barrier model developed will allow IMF manufactures to test foods for their ability to promote gut barrier maturity, ultimately reducing the incidence of necrotizing enterocolitis in IMF fed babies.

The benefits to policymakers are:
As a direct result of TOMI, our results can influence policy makers. A TOMI scientist has been invited to attend the Joint FAO/WHO Expert Meetings on Nutrition (JEMNU) on Nitrogen to Protein Conversion Factors for Soy-based and Milk-based Ingredients used in Infant Formulas and Follow-up Formulas.

The benefits to the scientific community:
This research provided a significant evidence base for the fate of nutrients in the upper gut and how processing can influence efficacy. The scientific highlights included the development of a semi dynamic model of the infant gut and this project was the first in the world to report the development of an infant gut barrier in vitro.

Summary of Staff Outputs

Research Output	Male	Female	Total Number
PhD Students	2	0	2
Post Doctorates	0	2	2

Summary of Academic Outputs

Research Outputs	Total Number	Details
Publications in Peer Reviewed Scientific Journals	15	1. Y Chen, M Callanan, L Giblin, J Tobin, A Brodkorb. 2022. Comparison of conventional heat-treated and membrane filtered infant formula using an in vitro semi-dynamic digestion method. Food & Function, 1;13(15):8158-8167. doi:10.1039/d2fo00342b 2. Y Chen, M Callanan, C Shanahan, J Tobin, LF Gamon, MJ Davies, L Giblin, A Brodkorb.2021. The use of membrane filtration to increase native whey proteins in infant formula. Dairy 2021, 2(4), 515-529; doi.org/10.3390/dairy2040041 3. Kondrashina A., Brodkorb A. and Giblin L. 2021. Sodium butyrate converts Caco2 monolayers into a leaky but healthy intestinal barrier resembling that of a newborn infant. Food & Function, 12, 5066-5076. DOI 10.1039/d1fo00519g. 4. P Myintzaw, V Pennone, O McAuliffe, M Begley, M Callanan. 2022. Correlation of organic acid tolerance and genotypic characteristics of Listeria monocytogenes food and clinical isolates. Food Microbiology 2022-06 DOI:10.1016/j.fm.2022.104004 5. SL Bavaro, G Mamone, G Picariello, M Callanan, Y Chen, A Brodkorb, L Giblin. 2021. Thermal or membrane processing for Infant Milk Formula: Effects on protein digestion and integrity of the intestinal barrier. Food Chemistry. Doi: 10.1016/j.foodchem.2021.129019. 6. L Nyhan, M Przyjalgowski, L Lewis, M Begley, M Callanan. 2021. Investigating the use of ultraviolet light emitting diodes (UV-LEDs) for the inactivation of bacteria in powdered food ingredients. Foods 10, 797. Doi. /10.3390/foods10040797 7. L Nyhan, D Field, C Hill, M Callanan, M Begley. 2021. Investigation of combinations of rationally selected bioengineered nisin derivatives for their ability to inhibit Listeria in broth and model food systems. Food Microbiology. 2021 Oct; 99:103835 doi: 10.1016/j.fm.2021.103835 8. L Nyhan, N Johnson, M Begley, P O'Leary, M Callanan. 2020. Comparison of predicted and impedance determined growth of Listeria innocua in complex food matrices. Food Microbiol. May; 87:103381. Doi: 10.1016/j.fm.2019.103381.Food Microbiology Vol. 87, article 1033815. 9. L Nyhan, M Begley, N Johnson, M Callanan. 2020. An evaluation of Lux technology as an alternative methodology to determine growth rates of Listeria in laboratory media and complex food matrices. Int J Food Microbiol Mar 16; 317:108442. doi: 10.1016/j.ijfoodmicro.2019.108442. 10. S Gilmartin, N O'Brien, L Giblin L. 2020. Whey for Sarcopenia; Can Whey Peptides, Hydrolysates or Proteins Play a Beneficial Role? Foods. Jun 5;9(6):750. Doi: 10.3390/foods9060750. 11. A Brodkorb, C Egger, L Alminger, et al. I Recio. 2019. INFOGEST static in vitro simulation of gastrointestinal food digestion. (https://rdcu.be/brEMd) Nature Protocols 14(4), 991-1014. doi:10.1038/s41596-018-0119-1. 12. E Arranz, AR Corrochano, C Shanahan, M Villalvad, I Jaimed. S Santoyod, MJ Callanan, E Murphy, L Giblin. 2019. Antioxidant activity of whey protein-based beverages: effect of shelf life and gastrointestinal transit on bioactivity. Innovat. Food. Sc. Eng. Tech. 57: 10229. doi.org/10.1016/j.ifset.2019.102209 13. L Giblin, A Süha Yalçın, G Biçim, AC Krämer, Z Chen, MJ Callanan, E Arranz and MJ Davies. 2019. Whey proteins: targets of oxidation, or mediators of redox protection. Free Radical Research. 2019;53(sup1):1136-1152. Doi: 10.1080/10715762.2019.1632445. 14. JA Tur., C Jacob, P Chaimbault, M Tadayyon, E Richling, N Hermans, CN dos Santos, M Diederich, L Giblin, M Elhabiri, C Gaucher, P Andreoletti, A Fernandes, M Davies, A Bartoszek, M Cherkaoui-Malki, 2019.Personalized nutrition in ageing society: redox control of major-age related diseases through the NutRedOx Network (COSTAction CA16112). Free Radical Research. 22:1-8. doi: 10.1080/10715762.2019.1572890. 15. ZF Chen, A Kondrashina, I Greco, LF Gamon, MN Lund, L Giblin, and MJ Davies. 2019. Effects of Protein-Derived Amino Acid Modification Products Present in Infant Formula on Metabolic Function, Oxidative Stress, and Intestinal Permeability in Cell Models. Journal of Agricultural and Food Chemistry 67(19):5634-5646.

Peer Reviewed Conference Papers	25	1. Alina Kondrashina, Andre Brodkorb and Linda Giblin. A novel in vitro model of healthy infant intestinal barrier with increased permeability. 7th International Food Digestion Conference ICDF2022. May 3-5. Cork, Ireland. Oral 2. Yihong Chen, Michael Callanan, Linda Giblin, André Brodkorb. Infant in vitro semi-dynamic digestion of conventional heat-treated vs. membrane filtered infant formula with an increased native whey protein content. 7th International Food Digestion Conference ICDF2022. May 3-5. Cork, Ireland. Poster 16. 3. A Kondrashina, L Giblin, Q. Zou, N.E. Regost, J Lane. Effect of infant milk formula processing on protein digestibility, bioavailability and functionality as compared to human milk. ESPGHAN 2022. 22-25 June Copenhagen Denmark. (Annual meeting of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition). Poster. 4. Alina Kondrashina, Linda Giblin, Jonathan Lane. Effect of whey to casein ratio in goat infant milk formulation on protein digestibility, amino acid bioavailability and health biomarkers. 7th International Food Digestion Conference ICDF2022. May 3-5. Cork, Ireland. Poster 62. 5. Cathal Dold, Yihong Chen, Hazel B. Rooney, Simona Bavaro, André Brodkorb, Peadar Lawlor and Linda Giblin 2022. Effect of processing of infant milk formula on growth performance, protein digestibility & gut barrier physiology in vivo. . 7th International Food Digestion Conference ICDF2022. May 3-5. Cork, Ireland. Poster 128. 6. Yihong Chen. Membrane filtration reduces the heat-load of infant formula and affects the semi-dynamic infant in vitro gastric digestion. Virtual International Conference on Food Digestion (#VICFD2021). 6 May 2021. Oral. 7. Cathal Dold, Hazel Rooney, Yihong Chen, Simona Bavaro, Elena Arranz, André Brodkorb, Peadar Lawlor and Linda Giblin. Oral flash presentation number P12. Processing influences protein digestibility of infant milk formula: a pig study. Virtual International Conference on Food Digestion. (#VICFD2021). 6 May 2021. Oral 8. Peter Myintzaw, Máire Begley, Nicholas Johnson and Michael Callanan. Assessment of Tunable Detection Laser Absorption Spectroscopy (TDLAS) equipment to detect the degree of spoilage non-invasively in intact aseptic food products. 35th EFFoST International Conference 2021 Healthy Individuals, Resilient Communities, and Global Food Security 1-4 November 2021, Lausanne, Switzerland. Poster. 9. Yihong Chen, Michael Callanan, John Tobin, Linda Giblin, Andre Brodkorb. Membrane filtration increases native whey proteins in infant formula and affects the in vitro gastric digestion. 4th Food Structure and Functionality Symposium. online. 19 Oct 2021. Oral. 10. Cathal Dold, Hazel Rooney, Yihong Chen, Simona Bavaro, Elena Arranz, André Brodkorb, Peadar Lawlor and Linda Giblin. Tracking protein digestion of infant milk formula in the upper gut. VistaMilk Conference 2021. Online 9-10 Mar 2021. Oral. 11. Colm Shanahan, Michael Callanan, Andre Brodkorb, Luke Gamon, Mick Davies, Linda Giblin. Determination of Advanced Glycation products in Infant formula produced by thermal or cascade membrane filtration. S9 page 28. Nutraceuticals in balancing redox status in ageing and age-related diseases. Belgrade Serbia, 2-3 March 2020. Oral. 12. Linda Giblin. Effect of processing on Gastrointestinal Digestion of Infant Milk Formula. 7th International Conference on Food Chemistry & Technology on 10 Nov 2020. (online) Oral. 13. Linda Giblin. Whey proteins: gastrointestinal digestion, bioavailability & bioactivity International Food Technology Conference SHIFT2020 online. 13-15 July 2020. Oral. 14. Yihong Chen, Michael Callanan, John Tobin, Linda Giblin, Andre Brodkorb. Cascade Membrane filtration reduces the heat-load of infant formula and affects the in vitro gastric digestion. 49th annual food conference. 15 Dec 2020 online. Oral. 15. Linda Giblin. VistaMilk Annual Conference Milk proteins: digestion, bioavailability & bioactivity. 3 June 2020. Oral. 16. Simona Bavaro, Fiona O'Mahony, Yihong Chen, Michael J. Callanan, Andre Brodkorb, Linda Giblin. Thermal or Membrane processing for Infant Milk Formula- Effect on protein digestion. 10th probiotics, prebiotics and new foods, 8-10 Sept. Rome 2019. Poster. 17. M Callanan, C Shanahan, J Tobin, A Brodkorb, A Coffey and L Giblin. Assessment of Microbial Quality of Membrane Processed Infant Formula. IAFP European Conference, Nantes, France. 24-26th Apr 2019. Poster. 18. Shanahan, C. Michael Callanan, Linda Giblin, Andre Brodkorb. Determination of Advanced Glycation End-products (AGEs) in infant formula produced by standard and alternative cascade membrane filtration processing. Launch of NUTRI research group, Cork Institute of Technology, 6th December 2019. Poster. 19. A Brodkorb. Relationships between structures of dairy-based matrices and digestibility within the gastrointestinal tract American Dairy Science Association Annual Meeting, 23-26 June 2019, Cincinnati, Ohio, USA. Oral

		20. A Brodkorb. Digestion Dairy proteins- impact of processing World Dairy Summit, 23-26 Sept 2019, Istanbul, Turkey. Oral. 21. A Brodkorb. A static in vitro protocol for the simulation of food digestion – INFOGEST 2.0 protocol. 6th International Conference on Food Digestion, 2-4 April 2019 Granada, Spain. Oral. 22. Shanahan, C.W., Giblin, L., Tobin, J.T., Brodkorb, A., Gamon, L.F., Davies, M.J., Coffey, A., Callanan, M. Determination of Advanced Glycation End-products (AGEs) in infant formula produced by standard and alternative cascade membrane filtration processing. 48th Annual Food Research Conference, University of Limerick, 16 Dec 2019. Oral 23. A Brodkorb. What can we do with milk proteins? 32nd EFFoST International Conference Nantes, France, 6-8 Nov 2018. Oral. 24. A Brodkorb INFOGEST Food Digestion workshop. Update on INFOGEST static in vitro digestion method. Lisbon 13 April 2018. Oral. 25. C Shanahan, L Giblin J Tobin, A Brodkorb, A Coffey, M Callanan. TOMI: Thermal Or Membrane processing for Infant formula. 46th Annual Food Research Conference 6-7 Dec 2017, Teagasc Food Research Centre, Ashtown Dublin. Poster.
PhD Theses	1	Yihong Chen successfully defended his PhD entitled 'The use of membrane filtration to increase native whey protein in infant formula, and effects on bioaccessibility and bioactivity' on 29 August 2022. MTU, Cork. External Examiner Prof Xiao Dong Chen
Training courses	1	TOMI PIs ran a 1-day training course on digestion and bioavailability to Industry Scientists (Ingredient Suppliers) on 02 Sept 2019.
Other	3	TOMI PI hosted two overseas postgraduate students in the lifetime of this project and supported a TOMI postgraduate student to work at University of Copenhagen, Denmark for 3 months: 1. TOMI PI Hosted PhD student Zhifei Chen May 7th to July 4th, 2018, University of Copenhagen Denmark. 2. TOMI PI Hosted PhD student Ariadna Gasa Falcon (8th April- 9th August 2018) Department of Food Technology, University of Lleid, Spain. 3. TOMI student Colm Shanahan Short term scientific mission to University of Copenghagen, Denmark (June -Sept 2019).
Book Chapter	1	Gaspard, S. J., & Brodkorb, A. (2019). The Use of High-Performance Liquid Chromatography for the Characterization of the Unfolding and Aggregation of Dairy Proteins. In J. J. McManus (Ed.), Protein Self-Assembly: Methods and Protocols (pp. 103-115). New York, NY: Springer New York.

International Conferences	2	1. 3-5 May 2022: Hosted 7th International Food Digestion Conference. 250 delegates of which 220 were from overseas. Cork, Ireland. The conference consisted of 5 sessions with 6 invited speakers, 24 oral presentations, 2 poster sessions with 136 posters. 2. 6-7 May 2021: Virtual International Food Digestion Conference 2021 (V-ICFD2021) online. This was recorded live on YouTube. It consisted of 7 sessions, 24 oral presentations & 24 flash presentations: Attendance: 49 different countries. 529 people for day 1, 310 people for day 2, 137 people for the flash presentations. 618 unique attendees across the 2 days with >1000 views on YouTube with an average view of approx. 15 minutes.

Intellectual Property

In 2020 we submitted an invention disclosure Teagasc IDF2020641 describing the development of an in vitro infant gut model. Teagasc offers in vitro semi dynamic digestion method as a service to industry Teagasc offers in vitro infant gut barrier as a service to industry.

Cascade membrane filtration is not a novel processing method and has been used by others. Therefore, the method cannot be IP protected.

Summary of other Project Outputs

Project Outputs	Details	Total No.
New Industry Collaborations	3 confidential Client contract projects were initiated with industry as a direct result of this project, approx. €100,000 funding Developed	3

Potential Impact related to Policy, Practice and Other Impacts

Impact	Details
Environmental Sustainability	Producing IMF by cascade membrane filtration will lower heating costs of production. The digestion, bio accessibility and bioavailability research capacity built in TOMI can offer a service to food manufacturers to test efficacy of nutrients, especially proteins, in food matrices as the consumer continues to look for sustainable environmentally friendly alternatives to meat and milk.
Socio-Economic	TOMI has produced an EU compliant IMF powder which is safe and of enhanced nutritional quality. This nutritional enhanced IMF will be off benefit to those babies fed IMF or IMF follow-on products. The in vitro infant gut barrier model developed will allow IMF manufactures to test foods for their ability to promote gut barrier maturity, ultimately reducing the incidence of necrotizing enterocolitis in IMF fed babies.
Industry	TOMI offers industry a next generation IMF. TOMI has delivered at pilot scale a safe IMF with enhanced digestion properties. The interest and relevance to industry is evidenced by industry funding of 3 follow-on projects and their sponsorship of €45,000 to the 7th International Food Digestion Conference hosted by TOMI scientists. Ireland's economic development was supported by TOMI, through the training of 4 skilful, well-educated scientists. As a direct result of TOMI, one researcher is employed in a full-time permanent position in industry, another is employed in a full-time permanent position in academia, and another has been awarded a PhD.
Other	TOMI impact on the scientific community is considerable with 1 PhD dissertation, 15 peer reviewed scientific publications, 19 presentations at international conferences, 6 presentations at national conferences, 1 book chapter and 1 invention disclosure. The impact of these publications is the strengthening of our international reputation which has resulted in our partnership with EU scientists to access EU funding (GiantLeaps and CirAlgae) and our leadership roles in EU consortia (INFOGEST and NutredOx COST Action).

Dissemination Activities

Activity	Details
Media Events	1. TV program: TOMI research on RTE series '10 Things to Know About' – Gut Health screened on 6th December 2021. 2. Newspaper article: Irish Examiner 20 Jan 2020' Research may give edge in global infant formula market' journalist Aileen Quinlin 3. LGiblin Live webinar Teagasc Research Insights 4th Nov 2020 webinar Teagasc Research Insights
Workshops at which results were presented	TOMI PIs ran a healthy food workshop with Older Adults at Cluain Dara Older Adult Day Care Centre, Fermoy 4-7 Nov 2019.

Public engagements	1. TOMI showcased at PubhD Cork Explain your research in a pub 12th Meeting (www.pubhd.ie) TOMI: Thermal Or Membrane processing for Infant formula 7 Feb 2019 2. TOMI showcased at Cork Discovers Event 27 Sept 2019 3. TOMI showcased at Moorepark Open Day 4 July 2017 4. TOMI showcased at Moorepark Open Day 3 July 2019 5. TOMI showcased at Moorepark Open Day 14-16 Sept 2021 6. TOMI showcased at Pint of Science 2021. Pint of Science organising committee. 17-20th May 2021. 7. TOMI showcased at A Day in the Life - Science Week - YouTube video. Online. 11th November 2021.
Popular press	Teagasc T-Research: A gentler approach to making infant formula 2019 V14:4:26-27
Education outreach events	1. 5 Oct 2017 Loretto Secondary School, Fermoy Cork, Career Guidance information session (Linda Giblin). 2. 11 Oct 2017 UCC undergraduate career day (Linda Giblin). 3. 30 Jan 2018 Colm Shanahan and Linda Giblin performed laboratory demonstrations to 5th & 6th class primary school children at Castlelyons National School, Cork. 4. 15 March 2018 UCC Food Science Graduates (L Giblin). 5. 23 Oct 2018 Loreto Secondary School Fermoy Career Day (L Giblin). 6. 27 Nov 2018 Linda Giblin delivered an invited lecture CIT 'Food digestion & Bioavailability' 4th year nutritional science students. 7. Linda Giblin Hosted MTU nutrition undergraduate student for 20 weeks from 20 March 2018. 8. Linda Giblin Hosted TY Female Student Loreto Secondary School Fermoy week of 19 Nov 2018. 9. Jan 2019 C Shanahan, STEM Education Primary School Workshop, Sundays Well National School 10. 10 Jan 2019 BT-Young Scientist Exhibition (Linda Giblin Andre Brodkorb) TOMI showcased at Teagasc Booth, RDS Dublin. 11. Linda Giblin Hosted TY Female Student Loreto Secondary School Fermoy week of 11th Feb 2019. 12. Nov 2019 Linda Giblin delivered an invited lecture CIT 'Food digestion & Bioavailability' 4th year nutritional science students. 13. 28 Feb 2020. Linda Giblin performed laboratory demonstrations to 5th & 6th class primary school children at Castlelyons National School, Cork. 14. 8-10 Jan 2020 BT-Young Scientist Exhibition (Andre Brodkorb), TOMI showcased at Teagasc Booth, RDS Dublin. 15. 8 Dec 2020 Linda Giblin delivered an invited lecture CIT 'Food digestion & Bioavailability' 4th year nutritional science students. 16. Linda Giblin Hosted TY Female Student Loreto Secondary School Fermoy week of 2-6 March 2020. 17. 30 Nov 2021 Linda Giblin delivered an invited lecture CIT 'Food digestion & Bioavailability' 4th year nutritional science students.

Knowledge Transfer Activities

Identify knowledge outputs generated during this project.	There were 4 main industrial knowledge outputs from this project (2 products and 2 methodologies): • 100kg Infant milk formula suitable for babies 0-6 months old was produced by cascade membrane filtration • 100kg infant formula suitable for babies 6-12 months produced by cascade membrane filtration • A semi dynamic model of the infant gastrointestinal digestion was developed. This is now offered as a Teagasc service to food manufacturers to track digestion of food in the infant gut. • An in vitro infant model of the gut barrier was developed. An invention disclosure was submitted. For Infant formula manufactures, this in vitro model will allow testing of infant formula for promotion of gut maturity. This should reduce the incidence of necrotizing enterocolitis in formula-fed preterm babies. The pharma industry can also use this in vitro model to test the permeability of oral drug compounds for infants. This model is offered as a Teagasc service. There were a considerable number of outputs to the academic community. ie 1 PhD dissertation, 15 peer reviewed scientific publications, 25 conferences presentations and 1 book chapter.
Identify any knowledge transfer activities executed within the project.	Knowledge transfer of this project to target end users was performed via Industry Stakeholder Advisory Panel. This panel consisted of 2 IMF manufacturers and 1 ingredient supplier. Initially at project start, non-disclosure agreements were signed with each panel member. Each member of the panel preferred knowledge transfer via one-on-one individual meetings. These one-on-one meetings were held at least once per year during the lifetime of the project. In addition, other IMF manufactures were given information on the project individually via 38 industry meetings by TOMI scientists, 1 Teagasc Gateway events (21 Nov 2019) and 1 industry event via DAFM-SFI research centre VistaMilk.
List any impacts resulting from the knowledge transferred during the project.	Impact of knowledge transfer to industry was evidenced by 3 follow-on industry confidential projects worth €100,000 and industry sponsorship worth €45,000 for the 7th International Food Digestion Conference hosted by TOMI scientists. Impact of knowledge transfer to academia is evidenced by the strengthening of our international reputation as leaders in protein digestion and bioavailability. This has culminated in 4 invitations to join EU consortia to access EU funding and 3 leadership roles in EU networks (INFOGEST and NutRedOx COST Action). Subsequently 2 HORIZON Europe proposals have been funded (GiantLeaps and CirAlgae). The impact of knowledge transfer to Teagasc has resulted in Teagasc investment in Food Biotest infrastructure worth €1.4m and instrumentation LC/MS/MS to continue to build capacity in this research area.

Section 3 – Leveraging, Future Strategies & Reference

Leveraging Metrics

Type of Funding Resource	Funding €	Summary
EU R&I programmes	€650,000.00	HORIZON Europe HORIZON-CL6-2021-FARM2FORK-01-12, Grant Number 101059632 GIANTLEAPS, 1 sept 2022 to 31 august 2026. Total €10,347,863, Teagasc allocation €650,000.
EU R&I programmes	€329,646.00	HORIZON Europe HORIZON-CL6-2021-CIRCBIO-01-09 1 Grant number 101060607 CIRCALGAE Oct 2022 to 30 sept 2026 Total: €10,332,894, Teagasc allocation: €329,646.
EU R&I programmes	€224,350.00	EU Horizon H2020-MSCA-IF-2019 GlucoMatchMaker grant number 898013
EU R&I programmes	€224,350.00	EU Horizon MSCA Cofund Career Fit Tool for blood glucose
EU R&I programmes	€106,000.00	EU HORIZON H2020-MSCA-RISE-2019 ENCAP4HEALTH (grant number 872019)
EU R&I programmes	€269,460.00	EU HORIZON H2020 Cofund Research Leaders 2025 (grant number 754380). Evaluation of Food structures.
EU R&I programmes	€2,500.00	EU-COST CA16112 NutRedox, Short term scientific mission Colm Shanahan
Exchequer National Funding	€222,573.00	EU-Marie Sklodowska Curie Career Fit Enterprise Ireland Horizon2020, FoodBIBS MF2018-015, 2018-2021, Teagasc €222,573
Exchequer National Funding	€223,730.00	FIRM-DAFM, MilkEVs 17/F/234, 2018-2022, total €595,0130, allocation Teagasc. €223,730.00.
Exchequer National Funding	€300,000.00	Science Foundation Ireland, VistaMilk 16/RC/3835, 2019-2024, total €40million, Teagasc Academic collaborator €300,000.00.
Exchequer National Funding	€150,000.00	FIRM-DAFM, U-PROTEIN, 2019PROG702 €2,999,866, TOMI scientists
Exchequer National Funding	€250,000.00	Teagasc Walsh Scholar funded Projects BIOPROTEIN and INFBAR
Exchequer National Funding	€968,038.00	DAFM-FIRM Infotech 2019R495
Exchequer National Funding	€70,000.00	CIT RISAM student scholarship Bacterial prediction
Other	€100,000.00	3 confidential client contracts to TOMI scientists, industry funded

Future Strategies

These methodologies developed in this project are at the cutting edge of science on how dietary protein is digested in the gut. As the consumer looks to alternative sustainable foods to replace meat and milk proteins, it is critical that digestion of these alternatives novel proteins is tracked and monitored for human health. As such and as a direct result of this project, TOMI scientists are part of a Horizon Europe project 'Giant Leaps' that aims to optimize future diets based on alternative proteins. TOMI scientists continue to engage with industry in this research space with €100,000 in client contract funding. To continue to build capacity in this area, Teagasc has also invested in Food Biotest infrastructure worth €1.4m to test protein digestion using pigs as the animal model, purchased LS-MS/MS instrumentation to identify dietary peptides during digestion and invested in 2 Walsh Scholarships to develop the infant gut barrier model and bring DIAAS (digestible indispensable amino acid score) method in-house.

Project Publications

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3. Kondrashina A., Brodkorb A. and Giblin L. 2021. Sodium butyrate converts Caco-2 monolayers into a leaky but healthy intestinal barrier resembling that of a new-born infant. Food & Function, 12, 5066-5076. DOI 10.1039/d1fo00519g. Impact factor 5.396.
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5. SL Bavaro, G Mamone, G Picariello, M Callanan, Y Chen, A Brodkorb, L Giblin. 2021. Thermal or membrane processing for Infant Milk Formula: Effects on protein digestion and integrity of the intestinal barrier. Food Chemistry. doi: 10.1016/j.foodchem.2021.129019.
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