Bioengineering Game Changing Technology: a horizon scan of therapeutics and drug delivery

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Conflicts of Interest

The authors declare no conflict of interest.

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Abstract

Background
Bioengineering bridges biology and engineering to develop technologies that address health-related problems, and it has therefore become one of the most impactful and fast-growing fields in healthcare. As this field continues to evolve rapidly, staying informed about promising technologies is essential for effectively applying new advancements to medical research and healthcare. In 2024-25, the NIHR Innovation Observatory (IO) undertook horizon scans to identify bioengineering applications in healthcare, with this report focussing on therapeutics and drug delivery. Early, horizon scanning enables the exploration of opportunities, leading to the timely adoption of new technologies.

Aim
This report aims to identify new areas and technologies within therapeutics and drug delivery, as well as to highlight emerging technologies or under-researched areas. The goal is to identify emerging bioengineered therapeutics and drug delivery with the potential to be game-changing; that is, to offer new solutions to health problems or re-purpose an existing technology for a new application.

Methods
This study used a novel, exploratory search method to generate a large number of results relevant to bioengineering. These terms were then first screened, cleaned, then grouped into clusters and visualised using VOSviewer, and finally those identified in VOSviewer as being particularly high frequency or new were further analysed by searching for applications in bibliographic databases and clinicaltrials.gov.

Results
The three most frequently-occurring and three newest keywords were identified, with the rationale that the most common keywords represent a strong signal and thus high research interest, and the newest represent potential novel game-changing tech. The three most frequent were “cell encapsulation”, “microRNA” and “nanofabrication”. Applications of these included encapsulated islet cells to treat type 1 diabetes, an microRNA prodrug to suppress tumour cell proliferation, and carbon dots to help bone defect healing. The three keywords defined as newest were “fucoidan”, “herpesviridae” and “siderophore”. Applications of these included dissolving microneedles to treat melanoma, a bioengineered vaccine for shingles, and the use of siderophores to move iron out of cancer cells.

Discussion
The methodology was targeted, rigorous and repeatable, ensuring the identification of technologies with potential game-changing applications. However, the reliance on a single bibliographic database and clinical trial registry and the preliminary nature of some findings highlights areas for further refinement.

Many of the technologies, such as those involving cell encapsulation, found were in the preliminary stages of development, and could be candidates for investment in translational research. Technologies at more advanced stages of development were highlighted to ensure that the correct regulatory processes are established, supporting their timely approval.

Conclusion

This horizon scan used a new method to identify technologies with the potential to provide new solutions to unmet needs within therapeutics and drug delivery. Some technologies could have important roles in addressing important national issues, such as donor shortages and antimicrobial resistance.

Introduction

Background

Bioengineering bridges biology and engineering to develop technologies that address health-related problems. Advances in both engineering and biology have allowed bioengineering to drive progress in many medical technologies, such as tissue regeneration drug delivery, and implants.[1] As bioengineering continues to revolutionise medical technology, it has become one of the most impactful and fast-growing fields in healthcare. The 2024 value of the global medical device market ranged from US$542.21 billion[2] to $810.4 billion[3], the tissue engineering market is projected to grow from $22.13 billion in 2025 to $43.13 billion by 2030[4] and the global nanotechnology market, valued at $8.78 billion in 2025, is predicted to reach $115.41 billion by 2034.[5] In addition, engineering biology is mentioned as one of several technologies that "hold significant promise" in the July 2025 NHS 10 Year Health Plan for England.[6] As this field continues to evolve rapidly, staying informed about promising technologies is essential for effectively applying new advancements to medical research and healthcare.

Therefore, in 2024-25, the NIHR Innovation Observatory (IO) undertook horizon scans to identify bioengineering applications in healthcare: focussing on tissues and medical devices, therapeutics and drug delivery systems, and genetically engineered organisms. Horizon scanning plays an important role in facilitating the integration of new technologies into healthcare. By identifying emerging technologies early, horizon scanning enables the exploration of opportunities, leading to the timely adoption of new technologies. As well as guiding research priorities, early identification of innovations enables health organisations to prepare for their implementation and minimises delays in patient access to innovative treatments.

Horizon scanning is particularly valuable in the rapidly advancing field of bioengineering, since its interdisciplinary and complex nature presents significant challenges in transitioning from research to clinical practice. Regulatory hurdles present a considerable challenge, as novel bioengineering approaches often fall outside traditional frameworks. As noted by Taylor (2014), these technologies span multiple domains, such as pharmaceuticals, medical devices, biologics and surgical procedures, which are each governed by distinct regulatory frameworks and, at times, different oversight bodies.[7] 3D bioprinting, a key example of bioengineering, involves living cells and is often bespoke, whereas existing regulatory systems are typically designed for mass-manufactured products, with separate pathways for handling living tissues and medical devices.[8] Another major obstacle is the "Valley of Death," the critical funding gap between early-stage research and successful clinical adoption. This is particularly pronounced in high-tech, science-intensive fields like tissue engineering, where early-stage development is costly and followed by the additional financial burden of funding large pre-clinical and clinical studies needed for regulatory approval and clinical uptake.[9] Ethical concerns further complicate

the landscape, particularly regarding issues of consent and ownership of donated cells and tissues.[10] The proactive approach of horizon scanning ensures that bioengineering continues to contribute to human health and address healthcare challenges.

Bioengineered therapeutics and drug delivery systems are rapidly advancing, with innovations in gene editing, synthetic biology and surface modification enabling the engineering of proteins, cells and microbes. Such strategies expand the natural capabilities of living systems, opening the door to novel and more effective cell-based therapies.[11]

Bioengineered therapeutics include a diverse range of engineered proteins, enzymes and antibodies, as well as larger macromolecular assemblies that mimic pathogens and cells, and immunostimulants.[12] Examples of applications include engineering live cells to counter antimicrobial-resistant pathogens, such as probiotic strains modified to better compete with or kill harmful microbes.[13] Bioengineered cytokines (messenger proteins), genetically modified bacteria and small molecule inhibitors of inflammation can act as anti-inflammatory agents with applications in cancer therapy.[14] Within immunotherapy, recombinant products and engineered cells (such as cancer vaccines, engineered cytotoxic cells, and engineered immunocytokines) demonstrate how bioengineering can harness the immune system to fight cancer.[15]

Drawbacks of traditional therapy include abrupt release, high toxicity, lack of specific targets, rapid degradation, and resistance.[16] These challenges highlight the need for more sophisticated approaches to improve drug performance and patient outcomes. Drug delivery systems address these limitations by allowing "entrance of a therapeutic material into the body [to increase] its efficacy and safety by controlling the rate, time, and anatomical location of drug release".[16] While synthetic drug carriers are widely studied, engineered natural particulates (such as microbes and mammalian cells) offer a promising alternative as they already possess their own, evolved delivery systems.[17] Nanoparticle-based drug delivery systems, including nanospheres, dendrimers and gold nanoparticles, offer advantages including improved permeability, retention and greater surface area.[17] However, they have not yet been widely taken up in clinical practice due to problems such as eliciting immune responses, poor delivery due to physiological barriers, drug toxicity to the non-targeted area and wider toxicity of synthesised materials.[17] There is therefore a gap in the market for new therapies that overcome these disadvantages.

Aim

This report aims to identify new areas and technologies within therapeutics and drug delivery systems, as well as to highlight emerging technologies or under-researched areas. Under-researched areas are defined in this context as those that appear less frequently in bibliographic searches, and which are relatively new to the field. By focusing on topics with limited current literature in areas with significant market potential and unmet clinical need, the

report seeks to capture opportunities that may benefit from increased research attention and investment.

The goal is to identify emerging bioengineered therapeutics and drug delivery systems with the potential to be game-changing; that is, to offer new solutions to health problems or re-purpose an existing technology for a new application. Here, we use the IO definition[a] of emerging technology as being the "horizon of the unknowns, [where] we identify potentially disruptive technologies that may have significant impact… This horizon is populated with patent intelligence and early research such as conference abstracts. Funders keen to progress early innovation are also a good source of signals. In some fields published and grey literature dealing with exploratory preclinical or very early clinical literature can be used to triangulate against these sources."

Scope

We followed the "HIP-D" framework (Horizon, Innovation, Population and Data source), as shown in Table 1. Interested parties could include funders, accelerators and catapults, Government departments, policy makers, regulators, health technology assessors, SMEs, patient groups and charities.

Framework item	Scope
Horizon	Emerging (from 15 years to market to present); all technology readiness levels; all clinical trial phases (including preclinical research)
Innovation	New technology; new application of existing technology
Population	Unspecified
Data source	Published literature (using Embase/Ovid). No study type limits; date limits January 2020-January 2025. Further searches also carried out in clinicaltrials.gov and PubMed.

Table 1 application of the "HIP-D" framework

Embase was selected as it is a large biomedical database and includes MEDLINE (the principle component of PubMed)[b] with extensive search limited options and an advanced search function.[c] The decision to begin the time threshold as 2020 was based on an article by The American Society of Mechanical Engineers.[18] This society is one of the leading global organisations developing codes and standards. It focuses on technical, educational and research issues of the engineering and technology community and one of its divisions focuses on bioengineering.[19]

[a] https://io.nihr.ac.uk/what-we-do/emerging-horizon/
[b] https://guides.library.uab.edu/lhldatabases/embase
[c] https://kemh.libguides.com/research/FAQ_Database_differences

Methods

As bioengineering is a broad topic which covers an extensive research landscape, this method was developed to transform complex bibliometric data into maps and keywords that provide direction for more efficient and targeted searches. The method is used in all three arms of the bioengineering project and is described in detail in a separate report. This section is an overview of the general method used as well as where methods specific to this arm were used.

The project used a novel, exploratory search method to generate a large number of results relevant to bioengineering. These results were then first screened, then grouped into clusters and visualised using VOSviewer, and finally those identified as being particularly high frequency or new were further analysed by searching for applications in bibliographic databases and clinicaltrials.gov. Finally, a preliminary analysis was carried out of the link between these keywords and unmet needs. The overall process is shown in Figure 1. Limitations are examined in the discussion section.

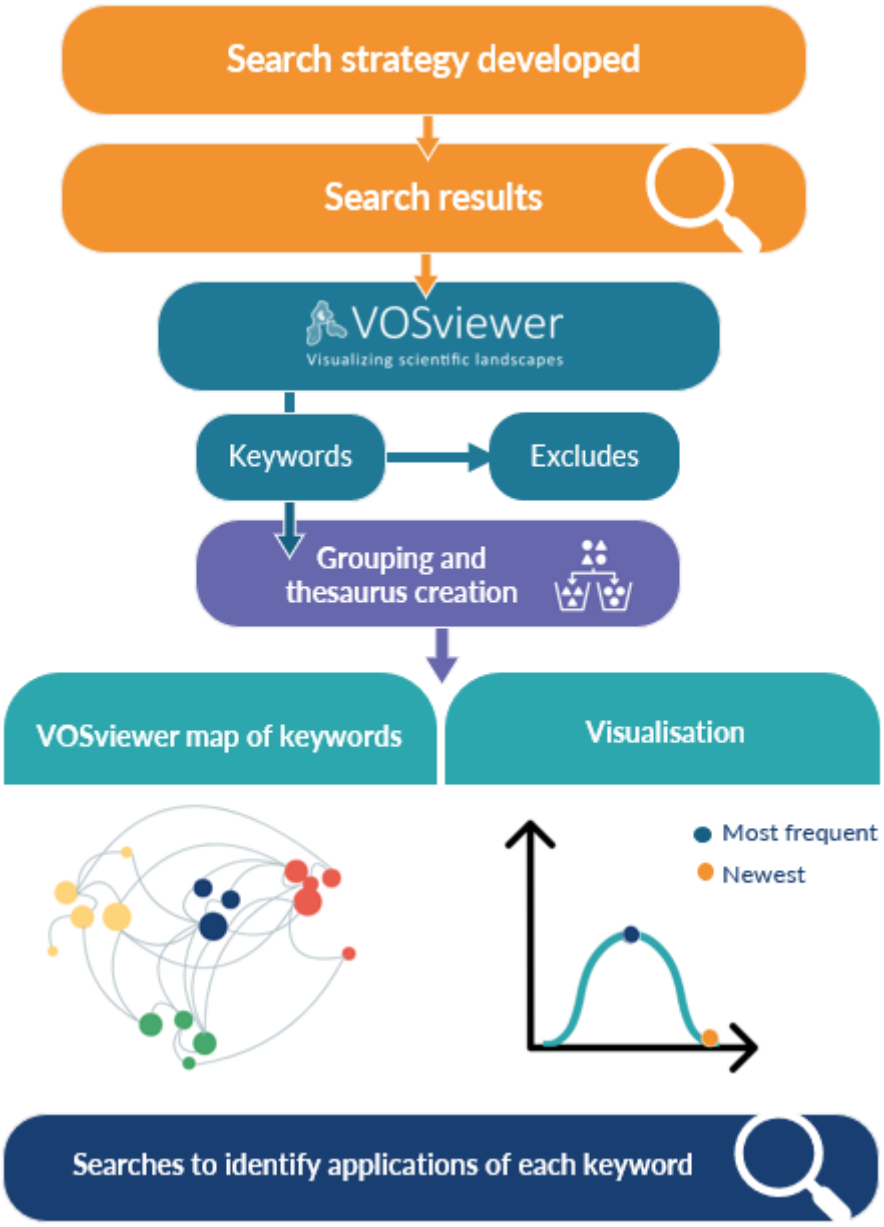

Figure 1 Overview of the method used. Image credit: Katie Twentyman.

VOSviewer

VOSviewer[d] is a free open-source bibliometric visualisation tool which creates maps of keywords based on co-occurrence data, enabling the examination of clusters of intelligence. This tool was selected because it offers an accessible way to summarise large datasets, such as those within the broad field of bioengineering, and to visualise patterns and key areas of

[d] www.vosviewer.com

interest. The keywords are located relative to each other, such that the distance between two is an approximate measure of their similarity within the set, and highly related terms are then indicated as clusters.[20]

The advantages of VOSviewer are that it supports a broad range of sources including PubMed, Lena and OpenAlex; it is user-friendly; and visualisations can be shared.[21] Although it has a small number of limitations, such as its inability to produce other visualisations such as tree maps, these are not relevant to the current study.

Search strategy

A bibliographic search was developed in January 2025 by an information specialist in Embase (OVID). Free-text English search strings were used, including terms for 'bioengineering', 'genetically engineered', and 'synthetic biology' developed through recent literature (see Appendix 1).[22-25] The search was subsequently peer reviewed by another information specialist.

Keywords

The RIS file generated from the bibliographic search were uploaded to VOSviewer (v 1.6.20). VOSviewer generated a keyword list of 4266 items which was downloaded into Excel.

Keywords were included in the "therapeutics and drug delivery" category if they met the following inclusion criteria:

1. Engineering biology acting as the drug/biomolecule or its delivery. Creation of engineered products that can target or treat diseases directly
2. There was evidence of its use in the past four years
3. There was evidence that it was being used for a specific application

Eligibility criteria

The exclusion criteria were:

1. A diagnostic, assay or imaging device, such as spectroscopy
2. A well-established technology, unless there was evidence that it had a new application
3. Very general terminology or redundant, such as "walking"
4. An irrelevant keyword, such as "side effect"
5. Any keyword not directly related to humans, such as "sheep" or "plant cell"

Thesaurus and creation of keywords list

A thesaurus list was compiled to clean the data and focus the keywords for a specific topic: in this instance, therapeutics and drug delivery. The thesaurus enhances the quality of the dataset as it removes duplicates, corrects errors and inconsistences, and consolidates different

versions of the same term (for example, due to UK/US English spelling variations) to ensure uniform treatment, improving accuracy for analysis.

To produce thesaurus lists specific to bioengineering and therapeutics and drug delivery, the keyword list was refined, with 259 relevant keywords included. A further 2201 keywords were excluded or grouped under a single term due to spelling convention or synonyms. This grouping was simply to place terms under a single umbrella term: the information could still be accessed. An example here is grouping the keywords “liver”, “liver cell”, “liver organoid” and “liver tissue” under the umbrella term “liver”. Finally, keywords relating to unmet needs were also identified. These included diseases such as “cancer”, areas of application within the body such as “inflammation” or an organ or tissues such as “kidney”.

Creation of VOSviewer maps

Once the selection and refinement process was completed, the thesaurus files were input into VOSviewer with the bibliographic search RIS file to produce a keyword map for analysis.

Data analysis

The most frequently-occurring keywords were identified, with the rationale that the most common keywords are those most frequently mentioned in the literature, representing a strong signal and thus high research interest (indicated with blue dot in Figure 2). We also selected the keywords that had the most recent publication date, representing novel technologies with the potential to be game-changing, indicated by the orange dot in Figure 2. This was done for all clusters and overall. The limitations of this method are discussed below.

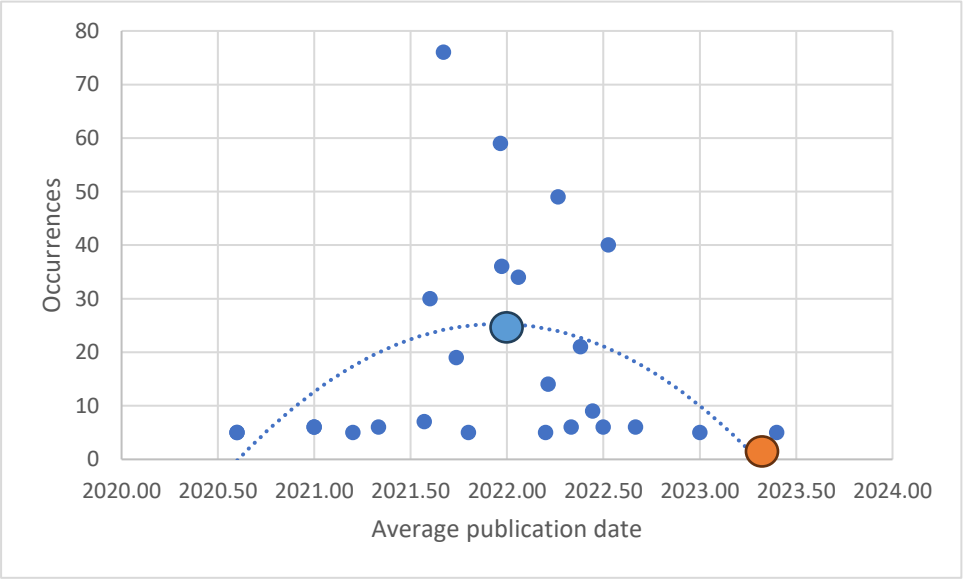

Figure 2 Distribution of occurrences of keywords against mean publication date, for a single cluster. Trendline is a 2nd order polynomial function. Example taken from Cluster 1 of tissues and medical

devices report.

Publication dates were extracted from VOSviewer as the mean value of all publication dates for that keyword. The mean dates of a sample of six keywords were compared to mean publication year in EndNote and the difference was found to be minimal and non-significant (7.2 months; p=0.357 by two-tailed t-test).

Search terms for further analysis of keywords

Applications of the most and least frequently-occurring new keywords were then searched for in the FDA[e], EMA[f] and MHRA[g] medical devices databases. The searches, which took place in September 2025, consisted of searching for the keyword itself. Most searches returned no results, and the few that did were largely irrelevant. The EMA search for Herpesviridae returned results for attenuated vaccines and the Shingrix recombinant vaccine (both of which also appear in later searches and are discussed further below). The MHRA search for siderophore returned a summary of product characteristics for Fetcroja, whose active ingredient is cefiderocol (also identified and described below).

These keywords were also searched for in three databases: 1) in May-June 2025 clinicaltrials.gov (including trial phase and primary completion date (PCD) as an indicator of technology readiness level); 2) the original Embase search in EndNote; and 3) since the Embase search was carried out in January 2025, PubMed was searched with date limits 1/1/2025 to 18/6/2025 to identify work published since the Embase search. Search criteria were as follows unless otherwise stated and up to five examples relating to therapeutics and/or drug delivery were found for each keyword per source. Primary research articles were prioritised over reviews, since the purpose of these is to review existing literature, rather than presenting cutting-edge findings. When included, reviews were carefully selected to ensure they presented findings into the latest developments.

1. clinicaltrials.gov: Other terms: *[keyword]* | Not yet recruiting, Recruiting, Active, not recruiting, Completed, Terminated studies | Study start on or after 01/01/2020

2. Embase (via EndNote): search for *[keyword]* in the Abstract field. Identified articles were then tagged with the keyword for ease of future retrieval and sorted by date. Searching began with the newest papers and abstracts were read to identify relevant technologies.

3. PubMed: search for *[keyword]* in primary research articles published since 1 January 2025. Results were then sorted by date, with the search starting at the newest article.

[e] https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfrl/TextSearch.cfm
[f] https://www.ema.europa.eu/en/search?
[g] https://products.mhra.gov.uk/search/

Inclusion criteria

Examples were only included where the technology itself formed part or all of the intervention under test, rather than being used as a placebo, vehicle or measurement technique. Included records related to therapeutics and drug delivery, with clear application to a medical or healthcare context. Protocols were excluded, as were records that described the development, preparation or improvement of the technology, with no mention of an application. Terminated trials were only included if the termination was due to reaching goal recruitment early.

Assessment of technology readiness level (TRL)

While identifying individual examples of applications for each keyword has merit, of greater utility is to map keywords to their technology readiness level (TRL), since this provides policymakers and funders with an overview of where technologies lie in the pipeline. TRLs are "a type of measurement system used to assess the maturity level of a particular technology"[h], and provide a common understanding of the status of a technology[i]. We used two methods to categorise TRLs: the first provided by UK Research and Innovation[j] as the investors of £8 billion of UK taxpayers' money each year into research and innovation[k]; and the second provided by[l] the Utrecht Health Seed Fund, who invests in science-based startups in life sciences/MedTech, digital innovation and sustainability. These latter definitions more clearly match TRL to clinical trial phase. A protocol to assign TRLs was agreed between members of the team and followed for each arm. We only mapped results from clinical trials due to both the volume and variety of results from bibliographic sources. The eligibility criteria were the same as those given in the Inclusion Criteria section above.

We used these definitions to map the keywords to TRLs as follows. First, if trial webpage contained the name of the technology, a brief Google search was performed to identify if it was already marketed for the indication on test: if it was, this was categorised as TRL9. If the technology was already marketed and a different application was being tested, the TRL was categorised based on the current trial. When stated, trial phase and status (for example completed phase III trial) were used to categorise each record. Trials which did not state the phase were categorised based on if the trial was of the safety or efficacy of the technology and its status. If the trial investigated both safety and efficacy, it was deemed a secondary trial. If the same technology was identified in more than one trial, it was only counted once, and the highest TRL taken. See Appendix B for the full protocol.

[h] https://www.ukri.org/councils/stfc/guidance-for-applicants/check-if-youre-eligible-for-funding/eligibility-of-technology-readiness-levels-trl/
[i] https://www.defproc.co.uk/insights/technology-readiness-level-trl-explained
[j] https://www.ukri.org/wp-content/uploads/2022/01/EPSRC-11012022-Technologyreadinesslevelsfrombasicresearchtoadoptionanddiffusion.pdf
[k] https://www.ukri.org/
[l] https://uhsf.nl/wp-content/uploads/2020/02/TRL_overview_UHSF_version20200206.pdf

Link between keywords and unmet needs

One goal of this project was to determine if the method could be used to detect potential applications of the identified technologies. Therefore, each of the six keywords was combined with a thesaurus for the unmet needs and used to create a map in VOSviewer (*Figure 3*).

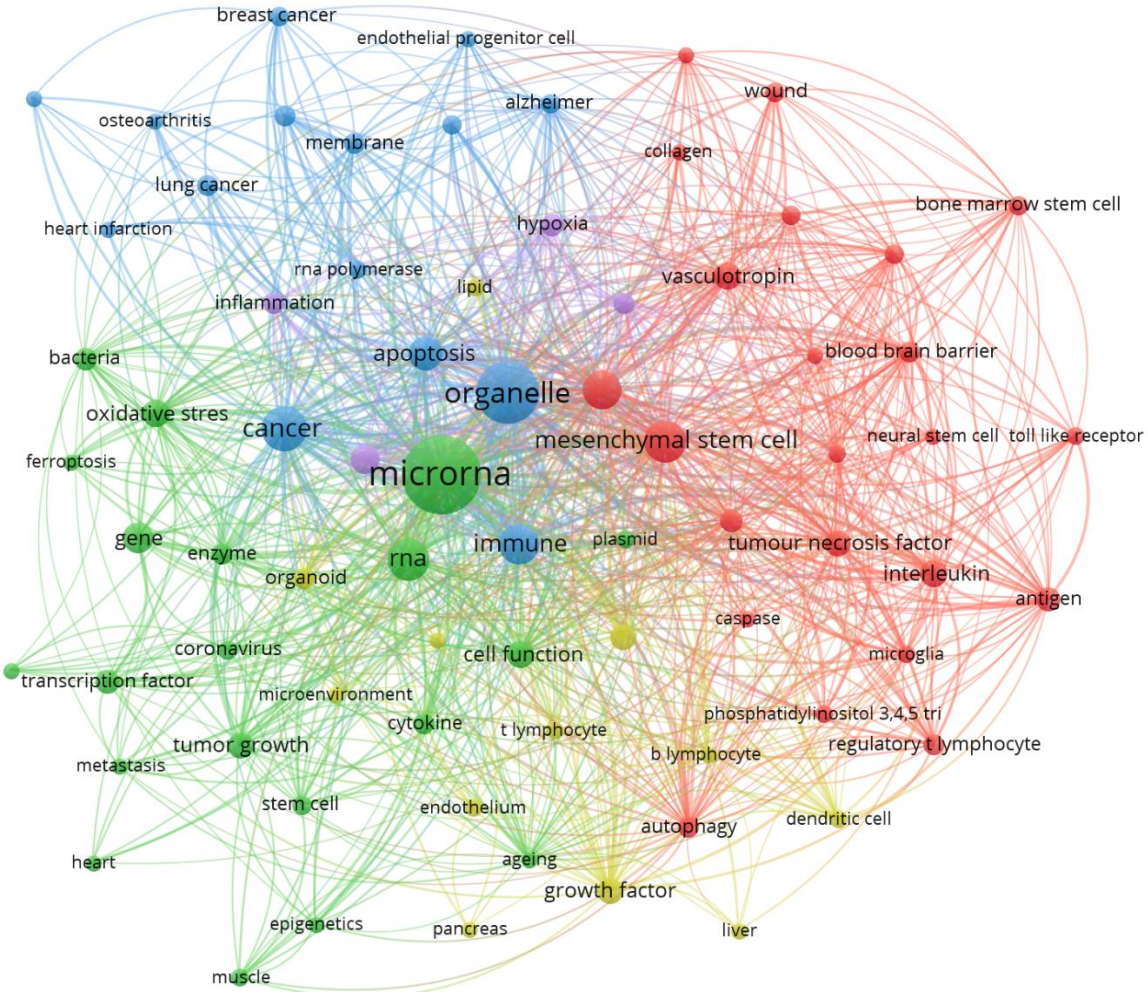

Figure 3 A VOSviewer map showing the links between a selected keyword (microRNA) and the identified unmet needs.

A thesaurus specific to unmet needs was created as described in the "Thesaurus and creation of keywords list" section. A library for each keyword was created by searching for it in the "keyword" field in Endnote, then exporting the library as a .txt file. A VOSviewer map was created (*Figure 4*), then the map and network files were exported as .csv files and converted to .xlsx files for analysis in Microsoft Excel. The network file gives a numerical value for the link strength between two nodes. The top three unmet needs were identified for each keyword for

further analysis: this involved searching for the unmet need in the database of clinical trials for research currently being undertaken to fulfil these needs/applications.

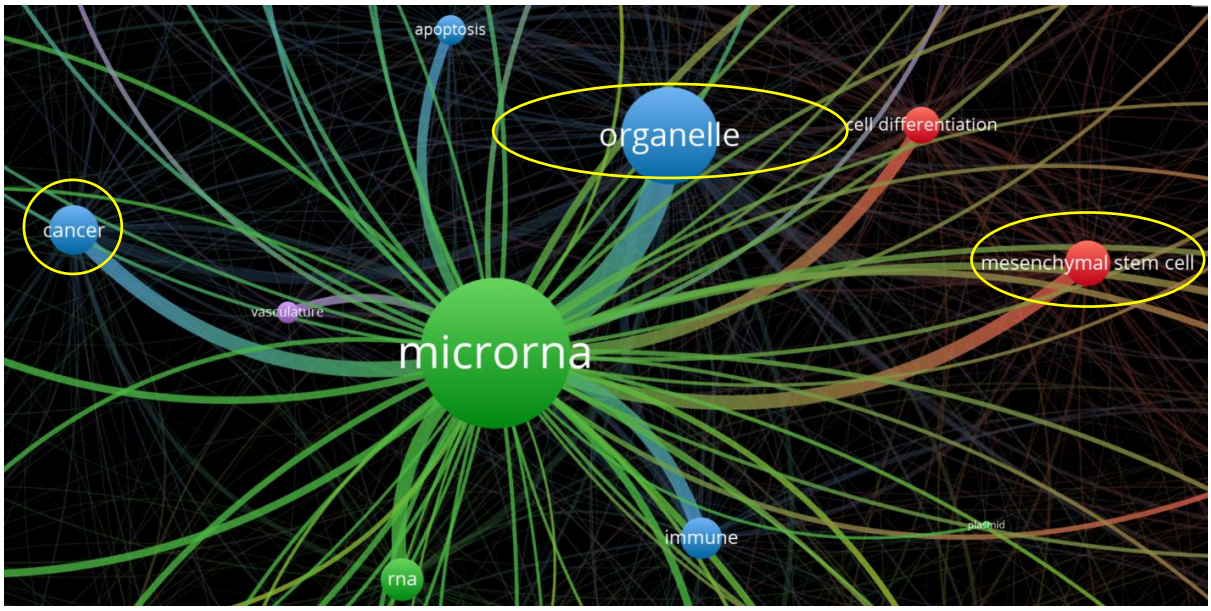

Figure 4 A close-up of the links between a selected keyword (microRNA) and the top three applications (cancer, organelle and mesenchymal stem cell). The dark background was selected to emphasise the width of the top three links.

The methodology limitations section in the Discussion highlights that this method demonstrated proof of concept. However, the second search for unmet need was limited to clinicaltrials.gov due to time constraints, which prevented a comprehensive bibliographic search. Consequently, the findings from this section should be regarded as preliminary evidence that supports the proof of concept established by this method

Expert engagement

The overall game-changing tech project comprises three arms: tissues and medical devices (the current project); therapeutics and drug delivery; and genetic engineering. These three arms were agreed at project outset with the Department of Health and Social Care.

Quality assurance

Various steps were taken to maximise the quality of the project. First, the search strategy was peer reviewed by a second, experienced information specialist. Secondly, a pilot screen was undertaken by all three reviewers (PA, RP and MF), who were blinded to the others' decisions.

This was followed by peer review, which helped to guide the groupings for the technologies found. The inter-rater agreement was 93.76%. While using a simple percentage has drawbacks, the figure is well above the 80% previously stated as the minimum acceptable interrater agreement.[26] Finally, the methods and preliminary results were discussed and peer-reviewed by a senior member of the IO leadership team.

Results

Figure 5 shows the overall visualisation of keywords, and the links between them, produced in VOSviewer. There are a total of 10 clusters, each represented in a different colour. Each cluster is made up of the circles ("nodes") that represent a keyword and the links between them (known as "edges"). The size of each node indicates its occurrence; and the size of each edge the strength of the link between two nodes.

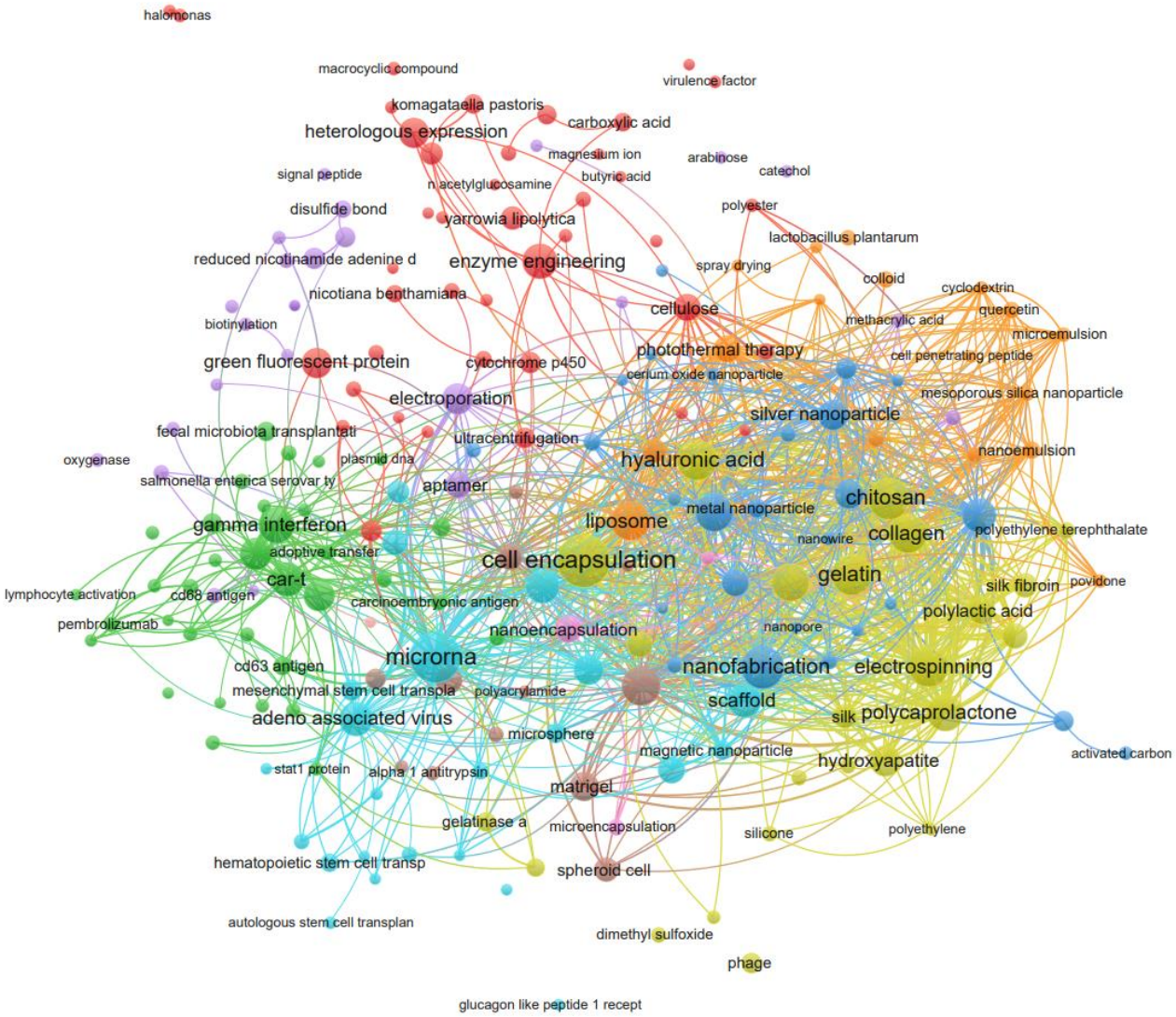

Figure 5 Overall drugs and therapeutics keyword visualisation in VOSviewer

A total of 205 keywords were extracted from 10 clusters (see Tables S1-10 in Appendix A). We focussed on the three most frequent keywords and three keywords with the most recent publication date, across all clusters (

Keyword (VOSviewer occurrences)	Mean publication date	CT.gov	Embase	PubMed
Cell encapsulation (119)	2022.32	71*	32*	65
MicroRNA (111)	2022.30	58*	32	4704*
Nanofabrication (76)	2021.67	0*	76*	75*
Fucoidin (5)	2023.20	8	6*	199
Herpesviridae (5)	2023.40	28*	6	1165
Siderophore (5)	2023.40	2	6*	264*

Table 1).

Keyword (VOSviewer occurrences)	Mean publication date	CT.gov	Embase	PubMed
Cell encapsulation (119)	2022.32	71*	32*	65
MicroRNA (111)	2022.30	58*	32	4704*
Nanofabrication (76)	2021.67	0*	76*	75*
Fucoidin (5)	2023.20	8	6*	199
Herpesviridae (5)	2023.40	28*	6	1165
Siderophore (5)	2023.40	2	6*	264*

Table 1 The search results (before screening) for the three most frequent (shaded in blue) and three newest keywords (shaded in orange). The asterisk represents where the numbers are from a more focused search.

Analysis of most frequent keywords

Note that the sub-headings for clinicaltrials.gov and PubMed are clickable hyperlinks directly to the search results page. The full hyperlink is given as a footnote for offline versions of this report.

Cell encapsulation

Clinicaltrials.gov[m]

[m] https://clinicaltrials.gov/search?start=2020-01-01_&aggFilters=phase:0%201%202%204%203%20NA,results:with%20without,status:not%20rec%20act%20com%20ter&term=cell%20encapsulation

No relevant results were revealed for "cell encapsulation", even after loosening the criteria[n] for study recruitment status. For example, trials involved conventional capsule filling or liposomal encapsulation, not cell encapsulation.

Therefore, the synonym "encapsulated cell therapy" was searched for[o], and a total of 71 trials were found, of which 65 reported the phase and six did not. Of the 65 trials that reported the phase, 63 were excluded for not meeting the inclusion criteria. None of the trials without phase were relevant. The two included were in TRL 6:

1. Eye implantation of NT-501 ciliary neurotrophic factor encapsulated cell therapy for the treatment of glaucoma (NCT04577300, phase 2, PCD August 2025, TRL 6)
2. Encapsulated porcine islet cells for xenotransplantation in patients with type 1 diabetes mellitus (NCT06575426, phase 1/2, PCD June 2027, TRL 6)

Embase

Only two records, which were not relevant, were found searching in the abstract. Therefore, a search was run in the keywords. Of the 32 records found, many examples relate to tissue engineering. While these are of interest, they are not relevant to therapeutics and drug delivery. Only one relevant record was found: this was a minireview discussing the encapsulation of pancreatic islet cells to advance islet transplantation without the use of toxic immunosuppressive drugs, to address donor islet shortage.[27] It concludes that though this has potential to provide a cure for type 1 diabetes, more advances and further studies are needed.

PubMed[p]

Of the 65 papers found, five relevant examples were:

1. Individuals with chronic kidney disease suffer from uraemia, a condition characterised by the accumulation of uremic toxins, such as p-cresol, in the blood. Encapsulation of a p-cresol degrading microorganism, *Thauera aminoaromatica* S2, was evaluated as a potential oral delivery method for intestinal p-cresol removal.[28]
2. Microencapsulation of Lactobacillus cells utilising the β-glucan-rich cell wall of *Saccharomyces cerevisiae*, offering enhanced probiotic protection.[29]
3. Three alternative tea polyphenols, gallic acid, epigallocatechin and epigallocatechin gallate, were bound to ferric ions, to fabricate metal-phenolic networks-coated *Lactobacillus rhamnosus* LGG. These alleviated ulcerative colitis by reducing myeloperoxidase levels, modulating cytokines profiles, and enhancing gut microbiota.[30]

[n] https://clinicaltrials.gov/search?start=2020-01-01_&aggFilters=phase:0%201%202%204%203%20NA,results:with%20without,status:not%20rec%20act%20com%20ter%20unk%20sus%20wit%20enr&term=cell%20encapsulation
[o] https://clinicaltrials.gov/search?start=2020-01-01_&aggFilters=phase:0%201%202%204%203%20NA,results:with%20without,status:not%20rec%20act%20com%20ter&term=Encapsulated%20cell%20therapy
[p] https://pubmed.ncbi.nlm.nih.gov/?term=%22cell+encapsulation%22&filter=dates.2025%2F1%2F1-2025%2F6%2F18

4. An encapsulation device featuring a spiral tubular semipermeable polyethersulfone membrane to house insulin-secreting islet-like spheroids. The device allowed for high density encapsulation, reaching therapeutic thresholds for type 1 diabetic patients.[31]
5. Encapsulated individual mammalian cells loaded with chemotherapy drugs, enhancing their targeting ability towards tumour sites and improving tumour-killing efficacy and reducing metastasis.[32]

Links to most common applications

Application	Strength of link
Extracellular matrix	13
Mesenchymal stem cell	10
Cell differentiation	7
Immune	5

Table 2 Applications with links to cell encapsulation

One of the included trials involved mesenchymal cells, but these were used as part of the therapeutic technology rather than as a target in the body: liver cells were co-encapsulated with mesenchymal stromal cells in alginate microbeads (NCT05491135). This trial was also linked to the immune system as the alginate protects the liver cells against the body's immune system, removing the need for immunosuppressive drugs.

MicroRNA

Clinicaltrials.gov[q]

The search in the 'other terms' field resulted in 214 trials; however, in most of these microRNA was a drug target (as mentioned in the trial summary), or measured as an outcome (mentioned in the primary outcomes table), rather than being part of the therapeutic technology. Therefore, to focus the search, 'microrna' was searched[r] for in the 'intervention/treatment' field, and 58 trials were found, of which 16 reported phase. Of these, 10 were excluded for not meeting the inclusion criteria. Of the six included, five were in TRL 6 and one was in TRL 5. None of the trials without phase were relevant.

The six relevant examples were:

1. AMT-162, an investigational gene therapy that encodes an artificial microRNA targeting the SOD1 gene in participants with amyotrophic lateral sclerosis (NCT06100276, phase 1/2, PCD September 2026, TRL 6)
2. ATX-01, a synthetic single stranded oligonucleotide designed to inhibit miR-23b in participants with myotonic dystrophy type 1 (NCT06300307, phase 1/2, PCD October 2024, TRL 6)

[q] https://clinicaltrials.gov/search?aggFilters=phase:0%201%202%204%203%20NA,results:with%20without,status:com%20act%20rec%20not%20ter&term=microrna&firstPost=_2025-06-15

[r] https://clinicaltrials.gov/search?start=2020-01-01_&aggFilters=phase:0%201%202%204%203%20NA,results:with%20without,status:com%20act%20rec%20not%20ter&intr=microrna

3. 4D-150, an Adeno-associated virus (AAV)-based gene therapy delivering a microRNA construct targeting VEGF-C in patients with diabetic macular oedema (NCT05930561, phase 2, PCD February 2028, TRL 6)
4. AMT-260 is a bioengineered AAV9 gene therapy delivering microRNA constructs to target the GRIK2 gene in patients with unilateral refractory mesial temporal lobe epilepsy (NCT06063850, phase 1/2, PCD November 2026, TRL 6)
5. SXRN, a naked plasmid DNA therapy encoding a miRNA sequence, targeting miRNA in patients with advanced solid tumours (NCT06736275, early phase 1, PCD September 2025, TRL 5).
6. 4D-150, an AAV-based gene therapy comprised of miRNA targeting VEGF-C and codon-optimised sequence encoding aflibercept is being tested in patients with neovascular age-related macular degeneration (NCT05197270, phase 1/2, PCD March 2027, TRL 6)

Embase

Of the 32 records found, five relevant examples were:

1. A humanised bioengineered miR-328-3p prodrug (hBERA/miR-328) suppresses tumour cell proliferation by downregulating GLUT1 and LAT1, impairing glucose uptake and suppressing the growth of highly-proliferative human osteosarcoma cells.[33]
2. A humanised bioengineered miR-124-3p prodrug targets plectin in lung cancer and osteosarcoma cells, that links cytoskeleton components and junctions. Efficacy and safety of this therapy was established in an aggressive experimental metastasis mouse model in vivo.[34]
3. A humanised bioengineered miR-1291 in combination treatment with 5-FU inhibited pancreatic cancer cell and organoid proliferation in vitro. In addition, miR-1291 mono- and combination therapy were effective to control tumour growth in pancreatic cancer patient-derived xenograft mouse models.[35]
4. A humanised bioengineered miR-34a-5p (hBERA/miR-34a) reduces cancer cell mitochondrial respiration capacity, which is accompanied by an increase of oxidative stress and elevated apoptotic cell death.[36]
5. A bone-targeted recombinant AAV carrying an artificial microRNA was used to silence Schnurri-3 (SHN3) expression to restore alveolar bone loss in mouse models of both postmenopausal and senile osteoporosis. It also enhanced bone formation and collagen production of human skeletal organoids in xenograft mice.[37]

PubMed [s]

Using 'microrna' as a search term found many papers focussed on using microRNA as biomarkers. Therefore, the search terms[t] 'microrna AND (therapy OR therapeutic OR treatment OR intervention)' were used. Of the 4,704 papers found, five of the most recent examples were:

[s] https://pubmed.ncbi.nlm.nih.gov/?term=microrna&filter=dates.2025%2F1%2F1-2025%2F6%2F18
[t] https://pubmed.ncbi.nlm.nih.gov/?term=microrna+AND+%28therapy+OR+therapeutic+OR+treatment+OR+intervention%29&filter=dates.2025%2F1%2F1-2025%2F6%2F18&sort=date

1. miR-200b-3p increases the sensitivity of paclitaxel in hepatocellular carcinoma treatment via inhibition of the drug-metabolising enzyme CYP1B1.[38]
2. miR-140-5p ameliorates atrial fibrillation in cardiomyocytes by suppressing inflammation and phosphorylation of Ca-handling proteins.[39]
3. miRNA-29a-5p attenuates haemorrhagic transformation and improves outcomes after mechanical reperfusion for acute ischemic stroke.[40]
4. miRNA-548d-3p represses non-small cell lung cancer growth by promoting pyroptosis through JAK2/STAT3 signalling.[41]
5. Small extracellular vesicles from human umbilical cord mesenchymal stem cells delivering miR-202-5p alleviate renal ischemia-reperfusion injury, a leading contributor to acute kidney injury.[42]

Links to most common applications

Application	Strength of link
Organelle	66
Cancer	33
Mesenchymal stem cell	31
Immune	30
RNA	30
Cell differentiation	26
Apoptosis	20
Vasculature	16
Cell function	15
Gene	15

Table 3 Top ten applications with the strongest links to microRNA

The three applications with the greatest links strengths to microRNA were: organelle (66), cancer (33) and mesenchymal stem cell (31) (Table 3). The only link between these top three and the six relevant trials was that trial NCT06736275 was evaluating a naked plasmid DNA therapy encoding a miRNA sequence in patients with cancer.

Nanofabrication

Clinicaltrials.gov[u]

No trials were found for "nanofabrication", even after loosening the criteria[v] for study recruitment status. Therefore, synonyms were searched including nanomanufact*, nanolithography and nanoscale manufacture, but these found no trials. Other synonyms such as nanotechnology manufact*, nanotech* manufacturing/manufacture or nano-scale

[u] https://clinicaltrials.gov/search?start=2020-01-01_&aggFilters=phase:0%201%202%204%203%20NA,results:with%20without,status:com%20act%20rec%20not%20ter&term=Nanofabrication

[v] https://clinicaltrials.gov/search?start=2020-01-01_&aggFilters=phase:0%201%202%204%203%20NA,results:with%20without,status:com%20act%20rec%20not%20ter%20enr%20sus%20wit%20unk&term=Nanofabrication

fabrication returned results; but the trials were related to using previously-made nano compounds rather than the fabrication itself: for example, making a dental prosthesis with added TiO_2 nanoparticles.

Embase

Only one record was found by searching in the abstract, and this did not relate to human health. Therefore, a search was run in the keywords. Of the 76 records found, five recent examples were:

1. A functionalised chitosan nanocarrier, with encapsulated CeO_2 and curcumin, as a pH-responsive drug delivery system for the treatment of sepsis. *In vivo* results show that this reduces bacterial burden and decreases inflammatory responses in a sepsis model.[43]
2. A dental floss thread, termed "nanofloss" uses polyphenol-based nanocoating to functionalise the floss thread with therapeutic agents, such as chlorhexidine gluconate to treat peroidontitis.[44]
3. Carbon dots are a type of nanoscale carbon-based material with antibacterial, anti-infective, osteogenic differentiation-promoting and gene-regulating properties: these may therefore help in bone defect healing.[45]
4. Organic curcumin and antimicrobial peptide loaded chitosan nanoformulations can successfully inhibit bacterial infections without disturbing intestinal microflora and could be used as an alternative to antibiotics.[46]
5. Thermoresponsive metal-phenolic network capsules that can be used to achieve temperature-controlled release of therapeutic cargo and hold potential for targeted drug delivery.[47]

PubMed[w]

A total of 192 papers were found, though many were not related to human health/disease. Therefore, the search terms[x] 'nanofabrication AND (therapy OR therapeutic OR treatment OR intervention)' were used. Of the 75 records found, four relevant examples were:

1. Cell walls of *Porphyromonas gingivali*, a pathogenic bacterium, were nanofabricated to form vesicles containing lipopolysaccharide and encapsulated doxorubicin. By combining chemotherapy, sonodynamic therapy and bacterial immunotherapy, the vesicles inhibited cancer growth.[48]
2. Triple-negative breast cancer-targeting aptamer-decorated porous silicon nanoparticles (pSiNPs) were used as targeted nanocarriers loaded with doxorubicin.[49]
3. Nanofabricated two-photon photosensitiser nanoparticles, termed MeTTh, enabled precise and efficient treatment of small-size glioblastoma *in vivo* under NIR-II laser irradiation.[50]

[w] https://pubmed.ncbi.nlm.nih.gov/?term=nanofabrication&filter=dates.2025%2F1%2F1-2025%2F6%2F18&sort=date

[x] https://pubmed.ncbi.nlm.nih.gov/?term=nanofabrication+AND+%28therapy+OR+therapeutic+OR+treatment+OR+intervention%29&filter=dates.2025%2F1%2F1-2025%2F6%2F18&filter=dates.2025%2F1%2F1-2025%2F5%2F31&sort=date

4. A miRNA delivery nanosystem, based on metal-organic frameworks and incorporating lipid coating, was developed to ensure effective miRNA-mediated gene therapy. This synergised with metal-organic framework-specific photodynamic therapy and pre-encapsulated doxorubicin chemotherapy to provide a multifunctional with therapeutic effectiveness against cancer cells.[51]

Links to most common applications

Application	Strength of link
Extracellular matrix	11
Cell differentiation	9
Stem cell	8
Wound	8
Cancer	7
Cell function	7
Vasculature	7
Inflammation	6
Immune	5

Table 4 Top nine applications with the strongest links to nanofabrication

The four applications with the greatest links strengths to nanofabrication were: extracellular matrix (11), cell differentiation (9), stem cell (8), and wound (8) (Table 4).

Analysis of least frequent but newest keywords

Fucoidan

Initial searches for this term revealed that "fucoidan" is the more widely-accepted term,[52] so this was used for searches instead. Since the same clinical trials were found using both search terms, the implication is therefore likely to be negligible. Fucoidan is a water-soluble sulphated polysaccharide with anti-cancer/-tumour, anti-proliferation, anti-inflammatory and immune-modulatory properties;[53] it also inhibits p-selectin, preventing neutrophil recruitment to the site of injury, and therefore has analgesic properties.[54]

Clinicaltrials.gov[y]

All trials found were investigating fucoidan in its non-bioengineered natural form. A total of eight trials were found, of which four reported the phase (Figure 6). Of the four trials that reported the phase, one was in TRL 5, two in TRL 6 and one in TRL 8. Of the four trials that did not report phase, two were in TRL 6 and two in TRL 7.

[y] https://clinicaltrials.gov/search?start=2020-01-01_&aggFilters=phase:0%201%202%203%204%20NA,status:not%20rec%20act%20com%20ter&term=fucoidan

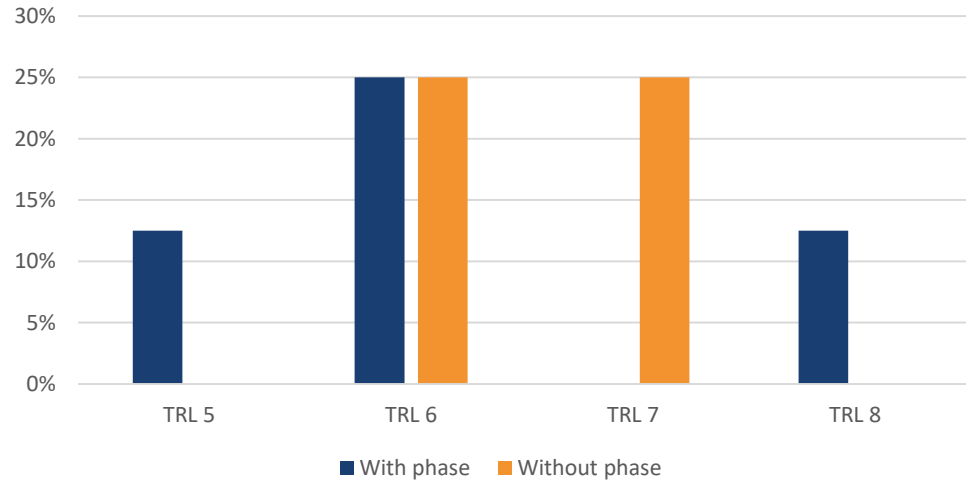

Figure 6 Proportions of each TRL for clinical trials investigating fucoidan

Five relevant examples were:

1. A dietary supplement, in which one of the active ingredients was fucoidan, aimed to enhance vascular function and exercise-induced vascular adaptations in type 2 diabetes (NCT05205005, phase 2/3, PCD March 2024, TRL 8)
2. Fucoidan-assisted eradication of *Helicopter pylori* and the effect on gastrointestinal flora (NCT05461508, phase 1/2, PCD June 2024, TRL 5)
3. The clinical effects and safety of fucoidan in the treatment of cancer patients with stage III/IV head and neck squamous cell carcinoma (NCT04597476, phase 2, PCD December 2024, TRL 6)
4. Using fucoidan to prevent chemotherapy-related fatigue in patients with gastrointestinal or gynaecological cancer (NCT06855524, phase 2, PCD February 2027, TRL 6)
5. The effects of fucoidan on prostrate health in males with benign prostatic hyperplasia (NCT06487871, phase N/A, PCD January 2025, TRL 7)

Embase

No results were found searching for either "fucoidan" or "fucoidin" in the abstract. Therefore, a search was run in the keywords. "Fucoidan" found no results, but "fucoidin" found six: of these, five were reviews and one was an editorial. Examples of applications within these were: wound healing,[55] biosensing,[56] cancer treatment,[57] and prevention of myocardial infarction.[58]

PubMed[z]

Of the 199 papers found, five relevant examples were:

1. A thiolated fucoidan-polydopamine nanocarrier was used to encapsulate a herbal therapeutic, tanshinone I. This resulted in a nanoplatform that optimised oral delivery

[z] https://pubmed.ncbi.nlm.nih.gov/?term=fucoidan&filter=dates.2025%2F1%2F1-2025%2F6%2F18&sort=date

of herbal bioactives, significantly enhancing their therapeutic efficacy against *Helicobacter pylori* infection.[59]

2. Bioactive dissolving microneedles composed of carboxymethylcellulose and fucoidan were developed to provide minimally-invasive treatment of melanoma. In skin models, they demonstrated complete dissolution within 12 min and strong anti-tumoral effects on melanoma cells.[60]
3. Fucoidan derived from *Saccharina japonica* was chemically engineered to have a low molecular weight and high degree of sulphation, enhancing its anti-obesity activity via gut microbiota regulation.[61]
4. Fucoidan-coated milk-derived extracellular vesicles were used to encapsulate anthocyanins and enhance delivery in gut models, reducing colitis-associated inflammation and oxidative stress.[62]
5. A multifunctional nanoparticle system incorporating fucoidan as a P-selectin-targeting ligand was bioengineered to enhance selective tumour binding, trigger ferroptosis and immunogenic cell death, and improve the efficacy of chemoimmunotherapy against metastatic cancer.[63]

Links to most common applications

Of the links between fucoidan and unmet needs, three had equivalent link strengths (2): blood clotting factor, breast cancer and coronavirus. No trials were found with links to these.

Herpesviridae

Clinicaltrials.gov[aa]

The search in the 'other terms' field resulted in 263 trials; however, in most of these Herpesviridae was a disease target, rather than being part of the therapeutic technology. Therefore, to focus the search, 'Herpesviridae' was searched[bb] for in the 'intervention/treatment' field, and 28 trials were found. Only one did not report phase, but the trial was not relevant.

Many of the relevant trials investigated technologies that were not bioengineered, but were live attenuated vaccines (three TRL 9, one TRL 8, two TRL 6) (Figure 7). There was one phase four trial investigating a vaccine called Shingrix, which contains a Herpesviridae glycoprotein and is currently approved by the EMA and FDA (TRL 9). Four trials were testing T3011, a genetically engineered oncolytic herpes simplex virus-1 (HSV-1) in multiple cancer types (two TRL 5, two TRL 6). One trial looked at an Epstein-Barr virus (EBV) glycoprotein (gp350) fused

[aa] https://clinicaltrials.gov/search?start=2020-01-01_&aggFilters=phase:0%201%202%203%204%20NA,status:not%20rec%20act%20com%20ter&term=herpesviridae
[bb] https://clinicaltrials.gov/search?start=2020-01-01_&aggFilters=phase:0%201%202%203%204%20NA,status:not%20rec%20act%20com%20ter&intr=herpesviridae

to ferritin to form a nanoparticle vaccine targeting Epstein-Barr virus (NCT05683834, phase 1/2, PCD April 2026, TRL 6).

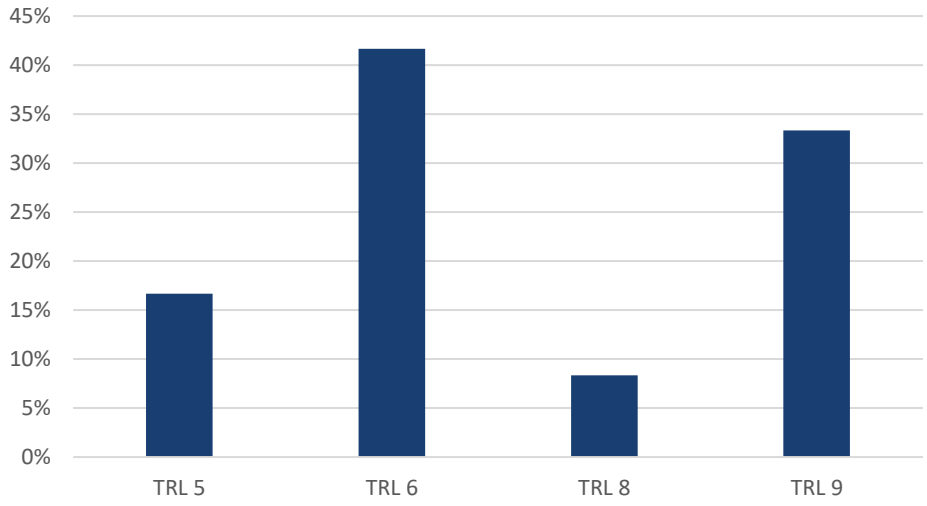

Figure 7 Proportions of each TRL for clinical trials investigating Herpesviridae

Embase

No records were found searching in the abstract. Therefore, a search was run in the keywords, and six records were found. However, in these, Herpesviridae was a disease target, not part of the therapeutic technology.

PubMed[cc]

1,165 results were found; however, in most of these Herpesviridae was a disease target, rather than being part of the therapeutic technology. Five examples using Herpesviridae as the technology were:

1. An EBV gL-gH344-ferritin nanoparticle vaccine induces robust and sustained specific humoral and cellular immune responses in mice, representing a potential immunotherapy for EBV-associated cancers.[64]
2. A multi-epitope vaccine for varicella zoster based on five varicella zoster virus (VZV) surface proteins was developed.[65]
3. EBV antigens LMP1 and LMP2A were bioengineered into B cells to induce T-cell immune surveillance that suppresses tumours, providing insights into cancer prevention.[66]
4. Five multiepitope mRNA vaccine constructs were designed using key viral proteins and bioengineering strategies to enhance immunogenicity, positioning them as promising candidates for HSV-2 vaccine development.[67]
5. A bioengineered VZV glycoprotein E and I fusion protein vaccine elicited stronger immune responses than the current leading vaccine, Shingrix, in mouse models.[68]

[cc] https://pubmed.ncbi.nlm.nih.gov/?term=herpesviridae&filter=dates.2025%2F1%2F1-2025%2F6%2F18&sort=date

Links to most common applications

The only links between Herpesviridae and unmet needs were binding site and immune, both with a link strength of 3. Many of the included trials had links to the term immune, as they involved vaccines designed to activate the immune system.

Siderophore

Siderophores are natural iron-chelating molecules produced and secreted by nearly all bacterial species to transport iron into the bacterial cell, which is essential for their survival and growth.[69] This mechanism can be exploited or mimicked to carry compounds across the bacterial cell, a strategy termed the *Trojan Horse* approach.[70]

Many records found below involved cefiderocol or deferoxamine, which are not bioengineered in the conventional sense but are bioinspired. Cefiderocol is a cephalosporin antibiotic conjugated to a catechol-containing siderophore moiety, allowing it to mimic natural siderophores and use bacterial active iron transport channels to cross the outer cell membrane to exert its bactericidal activity.[71] Deferoxamine is a semi-synthetic drug derived from the bacterial siderophore produced by *Streptomyces pilosus*.[72,73] Its role as an iron chelator means it could be used to treat various diseases, including cancer, where iron is essential for cancer cell proliferation,[74] and aneurysmal subarachnoid haemorrhage, where the breakdown of haemoglobin leads to iron overload and oxidative injury.[75]

Clinicaltrials.gov[dd]

Two trials were found, both with phases reported. One was excluded as its application was diagnostic. The other explored the safety and tolerability of cefiderocol in patients with cystic fibrosis as this antibiotic has potent activity against pathogens implicated in cystic fibrosis pulmonary exacerbations (NCT05314764, phase 4, PCD June 2024, TRL 8).

Embase

Only three records were found searching in the abstract, and only one was relevant. In this record, the core technology was a bacterial strain, of which the siderophore was utilised. *E. coli* Nissle 1917 was bioengineered to persist in tumours, where its natural siderophore, Yersiniabactin, acts as a transport agent for radiometals, enabling targeted delivery of radiotherapeutics to the tumour.[76] A search was run in the keywords, which resulted in six records, of which two were relevant reviews mentioning siderophore-conjugated compounds.[77,78]

dd

https://clinicaltrials.gov/search?aggFilters=phase:0%201%202%204%203%20NA,results:with%20without,status:com%20act%20rec%20not%20ter&viewType=Card&term=siderophore&start=2020-01-01_

Pubmed[ee]

Using 'siderophore' as a search term resulted in many non-relevant results including many focussed on agriculture. Therefore, the search terms[ff] 'siderophore AND (therapy OR therapeutic OR treatment OR intervention)' were used. Of the 254 records found, 5 new examples were:

1. Deferoxamine may mitigate the impact of *Porphyromonas gingivalis*-derived lipopolysaccharides on periodontal ligament stem cells by reducing iron levels, with implications in periodontitis.[79]
2. Deferoxamine can activate an otherwise bioinert nickel-iron nanomaterial to trigger targeted prostate cancer cell death by releasing toxic nickel ions, offering a precise and low-toxicity cancer therapy.[80]
3. A multifunctional microneedle system combining deferoxamine with anti-inflammatory nanocomposites is proposed to penetrate bacterial biofilms, modulate the burn wound microenvironment, and promote tissue regeneration and repair.[81]
4. A protocatechuic acid and deferoxamine-loaded polysaccharide-based immunoregulatory hydrogel was developed to promote advanced healing of full-thickness diabetic wounds.[82]
5. Cefiderocol demonstrated notable antibacterial against Gram-negative aerobic bacteria, with 83.4% of tested strains susceptible. When combined with phages, the two agents acted synergistically, showing potential as a strategy to tackle antibiotic resistance and biofilm-associated infections.[83]

Links to most common applications

The only links between siderophore and unmet needs were gene (3) and reactive oxygen metabolite (2). The included trial had no link with these unmet needs.

[ee] https://pubmed.ncbi.nlm.nih.gov/?term=siderophore&filter=dates.2025%2F1%2F1-2025%2F6%2F18&sort=date

[ff] https://pubmed.ncbi.nlm.nih.gov/?term=siderophore+AND+%28therapy+OR+therapeutic+OR+treatment+OR+intervention%29&filter=dates.2025%2F1%2F1-2025%2F6%2F18&sort=date

Discussion

Using a novel methodology, this report identified six bioengineering technologies with the potential to be game-changing, along with emerging trends, market readiness, and potential implementation hurdles.

Methodology

This report used a novel methodology: first, a comprehensive bibliographic search was undertaken, the results from which were uploaded into the visualisation tool VOSviewer. Secondly, VOSviewer generated a keyword list which was downloaded into Excel. This list was used to categorise keywords into the "tissues and medical devices" category (or to the "therapeutics and drug delivery" or "genetically engineered organisms" categories, which are the subjects of further reports), as a "non-specified new technology" or an application. The keyword list was refined, including creating a thesaurus to group keywords under a single term. The keyword list was used to create maps in VOSviewer, and then the most frequent and newest keywords were further analysed. Part of this further analysis involved linking technologies to an application; while this technique had limitations, it enabled proof of concept.

Methodology advantages

The advantage of this new method is that it is targeted and objective. The search was conducted in a relevant database using keywords developed from recent literature, ensuring a comprehensive dataset. If a more specific search was used, terms might be missed due to indexing or use of a synonym or alternative spelling, increasing the level of bias. This dataset was then analysed objectively, using pre-defined criteria to categorise the keywords found and then applying frequency and date filters. The approach of using the three most common and three most recent keywords can be replicated to identify key research within broad scientific fields. The keywords identified in this report can also be used for further targeted searches or to repeat the analysis in the future for more up-to-date insights.

This rigorous and objective approach ensured that the keywords found are those most likely to relate to game-changing technologies. It is a similar methodology that was adopted by three previous papers, all published by the same research group (Fujii et al. 2022,[84] Takata et al. 2022,[85] and Otsuka et al. 2023).[86] All three apply bibliometric analyses to horizon scanning, in the fields of drug development related to T cell immune response; AI-based medical products; and 3D bio-printing, respectively. Our approach differs in three key aspects. First, these three papers each focus on one specific area whereas our approach starts much broader, taking in all of bioengineering and then identifying keywords to subsequently undergo in-depth analysis. Secondly, the other papers analyse articles rather than keywords. Finally, they use publication date in a time series approach to identify key milestones in the history of each field, whereas we use publication date to identify the newest keywords. Therefore, while these three papers confirm the validity of the overall approach, the differences in aim and approach mean that an exact replication of the method would not have been appropriate.

Methodology limitations

This was a horizon scan to identify technologies of interest rather than to perform evidence synthesis: further work would be required to investigate each in depth. For example, a relatively brief literature search identified a study into a microfluidic device that could successfully maintain human glioblastoma tissue[87], which could replace current preclinical models. However, since the study did not include terms relevant to bioengineering, it was not found by our initial search. Therefore, future projects that include deeper analysis could use the keywords to perform more intensive and comprehensive searches. Additionally, we restricted the search initially to one bibliographic database (Embase/OVID). However, this database is comprehensive;[88] and in addition Donthu et al. (2021)[89] suggested using just one database to minimise potential human error during format conversion and data cleaning. The search was carried out in English only; further work could explore the possibility of including other languages. Also, only the clinicaltrials.gov registry was searched: future work could explore the use of other clinical trial registries.

Since this is a new methodology, it will inevitably have limitations which should be acknowledged and can be worked on in the future. We selected only the most frequent and newest keywords for further analysis; exclusion of the mid-range occurrences is acknowledged as a limitation as these could indicate translational technologies. However, selecting the top and newest keywords does present the advantage of being a repeatable method as these are defined points. Furthermore, analysis of the mid-range immediately presents the question of whereabouts the range should begin and end. In addition, the selected keywords provide a starting point for further searches into their application, rather than being presented as the game-changing technologies themselves: it is these searches that identify the latest publications regarding possible applications of the technology. Finally, the searches for these keywords can easily be performed again to obtain updated information: either to monitor the progress of previously-identified technologies or to identify new ones.

The methodology used to identify links between technologies and unmet needs was experimental but demonstrated proof of concept. The main limitations concerned the searches for the keyword in Endnote: first, this library contained keywords from across the whole bioengineering project and therefore some that were identified were not relevant to therapeutics and drug delivery and may for example have related more to tissues and medical devices. However, the identified technologies are still likely to have strong links to unmet needs across the whole of bioengineering and thus should not be discounted. Secondly, the keywords identified were based on a body of records published before January 2025, and therefore keywords in records published since that date do not appear in this analysis. Time constraints prevented the searches from being re-conducted. However, the method allows the keywords identified in the initial search to be reused to repeat the analysis at any time, providing more up-to-date insights. Thirdly, the analysis assumes that keywords represent technologies, and yet secondary searches showed that a technologies' primary identity was often something different, for example, a drug target or an outcome measure. Therefore, a high occurrence of a keyword did not necessarily reflect high occurrence of its use as a technology. For example, microRNA would not have yielded as many occurrences if only papers exploring microRNA as

a technology were included. Thus, caution should be taken when making inferences from keyword occurrences, as the method served primarily as a means of identifying potential technologies for deeper analysis rather than providing a direct measure of their prevalence. Therefore, while this iteration of the method has limitations, their solutions are straightforward.

Findings and implications

Cell encapsulation

Very few relevant clinical trials were found for cell encapsulation, possibly due to specific vocabulary used in clinical trials. Another possible reason is that cell encapsulation is often used to replace tissues, so many trials were excluded due to being classified into the tissues and medical devices category. As mentioned above, the library contained keywords from across all three categories and so occurrence of this word may be high due to its common use in tissue engineering. Even the two clinical trials highlighted in this report sit at the interface between drug delivery and tissue engineering as they rely on engineered tissue technology but deliver therapeutic molecules.

The bibliometric analysis resulted in more relevant examples, consisting of mostly preclinical studies, which may suggest that technology use in therapeutics lies more of the initial stages of development, with not many technologies reaching trial stage. Links between cell encapsulation and the extracellular matrix (ECM) may arise because encapsulation strategies often use biomaterials designed to mimic or interact with the ECM.

Applications of this technology spanned a broad spectrum of conditions, such as diabetes, glaucoma, liver failure, kidney diseases, ulcerative colitis and cancer. Technologies covered encapsulation of both microorganisms and mammalian cells, though clinical trial records found only looked at mammalian cell encapsulation, perhaps highlighting the additional regulatory complexity and biosafety considerations associated with translating microorganism-based encapsulation into clinical use. Two examples focussed on encapsulation of probiotic bacteria to improve gut health. Both a review and a paper highlighted the use of encapsulated islet cells to treat type 1 diabetes, highlighting a possible unmet need. Due to a growing diabetes population, diabetes is a NICE priority topic for 2024 to 2025.[90] Although outside the remit of this repot, a large number of technologies were found in the tissues and medical devices category, highlighting the potential of cell encapsulation to help alleviate future donor shortages. Even within the area of therapeutics and drug delivery, islet cells are available only in limited supply.[91] This scarcity highlights the importance of developing encapsulation approaches that can maximise the utility of available cells and ensure wider access to transplantation and cell-based therapies. By addressing donor shortages, advances in cell encapsulation could reduce dependence on organ donation systems, expand treatment availability, and ultimately improve equity and sustainability in healthcare worldwide. It is recommended that regulatory and approval processes for cellular therapies should be strengthened in preparation for their clinical application. Regulatory frameworks could be adapted by establishing clear guidelines for the evaluation and approval of cell encapsulation technologies. This could include streamlined processes for preclinical testing and clinical trials, as well as incentives for research and development in this area.

MicroRNA

Of the six trials found for microRNA, five were identified as TRL 6 and one as TRL 5, indicating that microRNA is mostly in the initial stages of clinical development. This is supported by the fact that the five identified Embase records were preclinical studies, investigating the technology in animal models or cells. These five records focussed on cancer indications, and along with the one cancer trial in TRL 5, suggests microRNA applications for cancer are in the preliminary stages. The strong link to cancer as an unmet need further emphasises cancer as a target for microRNA research.

Three of the trials looked at neurological conditions. Neurology is a NICE priority topic for 2024 to 2025.[90] Interestingly, the conditions tested in these trials tend to be chronic and worsen with time. The Global Burden of Disease 2021 studies highlighted neurogenerative diseases to be emerging as a significant burden to global health, linked to the demographic shift toward an ageing population.[92,93] MicroRNA technologies could represent a promising avenue for the treatment of these conditions. Another trial looked at advanced solid tumours, which are also difficult to treat and require high cost/high risk treatments. This suggests that microRNA technologies may provide options for patients who have the greatest need and have few other options. Recent publications indicate the broadening scope of microRNA research, with several other conditions appearing in the more recent PubMed search, such as ischemic stroke and atrial fibrillation. Overall, microRNA technologies are associated with high cost and complexity,[94] which must be taken into account to ensure that sufficient resources and infrastructure are in place when preparing for their development and market introduction, particularly given their potential in hard-to-treat conditions. International collaboration, through shared research infrastructure, harmonised regulatory pathways, and joint funding initiatives, could accelerate the development of microRNA-based therapies by enabling data sharing, reducing duplication, and supporting equitable access to emerging treatments worldwide.

Nanofabrication

No relevant trials were found, so it was not possible to link to unmet needs or determine TRLs. Future research could make use of alternative clinical trial registries. It is clear from the bibliographic results that nanofabrication and nanotechnology have a large scope and potential for applications, from bone defect healing to periodontitis. The most recent papers, found on PubMed, focussed on treatments for cancer, suggesting that this may be a current and new area of interest. The co-occurrence of the keyword ‘wound’ indicates applications in tissue repair and healing, while its link with ‘stem cell’ suggests that nanofabrication techniques may be used to encapsulate or deliver stem cells for these regenerative purposes.

Fucoidan

Fucoidan in its natural non-engineered form was investigated within the identified clinical trials, whereas bibliographic searches revealed several bioengineered examples. This may be because natural fucoidan has a long history of human use as a dietary component, making it easier to

progress into clinical trials due to its established safety profile, while bioengineered fucoidans have a less well-known safety profile and so are still largely at preclinical or early-stage research. Additionally, bioengineered fucoidans require more complex processing than natural fucoidan. Key barriers include limited understanding of how structural modifications affect biological activity and safety, and the need for standardised manufacturing processes to ensure reproducibility. Overcoming these barriers will require strong investment in resources and infrastructure. Another reason to focus on this technology is that existing clinical evidence on natural fucoidan could provide a strategic foundation for accelerating the development of bioengineered variants.

Herpesviridae

With the exception of the trial for Shringrix, an already approved, recombinant vaccine made from Herpesviridae glycoprotein, trials investigating bioengineered therapeutics containing Herpesviridae were in the earlier stages of clinical development (TRL 5 and 6). This is supported by the fact that the five identified Embase records were preclinical studies, investigating the technology in animal models or cells. One of the trials found that a new vaccine elicited stronger immune responses than Shringrix in mouse models. The main applications for Herpesviridae technologies were vaccines and cancer treatments. The NHS 10 year plan states "We will prioritise and deliver new vaccines that help prevent AMR [antimicrobial resistance] progressing"[6] and so the engineered vaccines identified here represent a strategic area for research investment. Additionally, given their underlying viral engineering approach, these technologies could also be adapted for use against other infectious diseases, offering flexible tools for rapid vaccine development in response to emerging pathogens.

Siderophore

Many of the siderophore-based therapeutics identified involved bioinspired cefiderocol and deferoxamine, inspired by biological systems with synthetic or semi-synthetic origins. This represents important research in the therapeutic field, but these compounds are not classed as bioengineered in the conventional sense, as they do not involve direct modification of biological organisms or genetic material. However, given the UK Government's 5-year action plan on AMR and its promise to invest in innovation,[95] along with the potential role of cefiderocol in addressing AMR, prioritising research and funding in this area may be warranted. Within the bioengineering field, a noteworthy innovation uncovered in this report was the use of an engineered *E. coli* strain's natural siderophore to act as a transport agent for radiometals in tumours, allowing for targeted delivery of radiotherapeutics.[76]

Conclusion

This report identified six bioengineering technologies currently under research. Cell encapsulation as a therapeutic remains in the preliminary stages of development but spans a wide range of potential applications, including an important role in addressing donor shortages. Similarly, microRNA technologies, though still at a preliminary stage, hold considerable promise for treating conditions with a high unmet need that are otherwise difficult to manage. It should be considered that naturally occurring molecules can be improved upon with bioengineering,

an example being the polysaccharide fucoidan, which is currently being studied in relation to cancer and gastrointestinal disorders. Finally, both Herpesviridae and siderophore technologies show potential for combating AMR, a UK and global priority.

Technologies highlighted as remaining in the preclinical research stage should receive greater investment in translational research and supporting infrastructure, to ensure their progression towards clinical trials rather than stagnation. For those technologies at a higher TRL (7-8), we recommend ensuring that the regulatory and approval processes are adequate and there is sufficient expertise for the specific technologies to enable their approval. International regulatory harmonisation could streamline the approval process for bioengineering technologies by establishing consistent standards and requirements across different regions. This would facilitate global collaboration and accelerate the adoption of innovative therapies.

The study underscores the importance of early identification and strategic investment in emerging bioengineering technologies to overcome interdisciplinary and regulatory barriers. By focusing on high-potential areas and fostering collaboration across research, industry, and regulatory bodies, these innovations can be accelerated to clinical practice, ultimately improving patient outcomes and addressing unmet healthcare needs.

Broader implications include the necessity for robust funding mechanisms, streamlined regulatory pathways, and ongoing horizon scanning to ensure the timely adoption of game-changing technologies. This proactive approach will not only enhance healthcare delivery but also position bioengineering as a cornerstone of future medical advancements.

Other information

The raw data used in this report can be made available on reasonable request.

Appendix A: keywords by cluster

The analysis of each cluster is shown in the following sections. The most frequent keywords are highlighted in blue, and the least frequent new keywords highlighted in orange. A total of 205 keywords were extracted.

Cluster 1

Keyword	Links	Total link strength	Occurrences	Avg. pub. year
Enzyme engineering	28	39	49	2021.92
Green fluorescent protein	39	41	38	2021.47
Heterologous expression	17	26	36	2021.81
Cellulose	49	88	30	2021.23
Yarrowia lipolytica	6	7	22	2021.82
Corynebacterium glutamicum	15	23	20	2021.35
Untranslated rna	16	37	19	2022.42
Cytochrome p450	18	19	18	2021.89
Ultracentrifugation	18	28	17	2022.47
Polyketide	9	11	15	2021.47
Komagataella pastoris	13	17	15	2021.67
Carboxylic acid	17	19	13	2022.00
Nicotiana benthamiana	10	11	12	2021.50
Rna vaccine	19	20	11	2022.00
Carboxymethylcellulose	19	21	11	2022.45
Angiotensin converting enzyme 2	8	8	10	2021.90
Lycopene	10	11	10	2022.00
Citric acid	13	15	9	2021.78
Rna binding protein	9	14	9	2022.44
Chemoluminescence	16	18	9	2022.56
Halomonas	3	8	7	2020.86
Recombinant plasmid	7	8	7	2021.57
Transcription factor nrf2	9	13	7	2022.14
Polyester	25	31	7	2022.57
Macrocyclic compound	1	1	7	2023.00
Halomonas bluephagenesis	2	7	6	2021.00
Multi walled nanotube	14	18	6	2021.00
Aspergillus nidulans	3	4	6	2021.33
Electromagnetic radiation	6	6	6	2021.33
Virulence factor	11	11	6	2021.50

Sialylation	4	4	6	2021.67
Integrin	6	6	6	2022.17
High mobility group b1 protein	10	14	6	2023.00
N acetylglucosamine	8	8	5	2021.60
Butyric acid	3	3	5	2021.80
Magnesium ion	2	2	5	2021.80
Magnetite	18	20	5	2021.80
Protein cross linking	5	5	5	2022.20
Protein rna binding	8	9	5	2022.20
Sialic acid	6	6	5	2022.20
Siderophore	2	2	5	2023.40

Cluster 2

Keyword	Links	Total link strength	Occurrences	Avg. pub. year
Gamma interferon	64	125	53	2021.83
Car-t	58	104	47	2021.77
Cd8+ t lymphocyte	45	84	42	2021.79
Optogenetics	14	18	39	2021.54
Fecal microbiota transplantation	9	10	15	2022.00
Immune checkpoint inhibitor	26	36	15	2022.60
Immunomodulating agent	17	23	13	2021.92
Cd63 antigen	28	37	13	2022.00
Bifidobacterium	10	13	10	2021.20
Carcinoembryonic antigen	38	46	10	2021.50
Pembrolizumab	19	33	10	2021.70
Rituximab	19	25	10	2021.70
Granulocyte colony stimulating factor	23	29	9	2020.89
Salmonella enterica serovar typhimurium	9	11	9	2021.56
Adoptive transfer	22	26	9	2021.67
Solid lipid nanoparticle	35	50	9	2021.78
Tumor necrosis factor related apoptosis inducing ligand	19	21	8	2021.38
Cd19 antigen	15	25	8	2021.50
Hla dr antigen	30	35	8	2022.13
Protein bax	11	13	8	2022.38
Granulocyte macrophage colony stimulating factor	18	23	7	2020.86
Protein tyrosine kinase	9	10	7	2020.86
G protein coupled receptor	7	8	7	2021.14

Prostaglandin e2	11	13	7	2021.29
Gamma interferon inducible protein 10	10	17	7	2021.43
Virus particle	5	5	7	2021.71
Stat1 protein	14	21	7	2021.86
Plasmid dna	18	18	7	2022.43
Antibody labeling	8	8	6	2022.00
Atezolizumab	9	18	6	2022.00
Cytotoxic t lymphocyte antigen 4	18	22	5	2021.00
Fibroblast growth factor	11	11	5	2021.80
Lymphocyte activation	5	6	5	2021.80
Monocyte chemotactic protein 1	5	5	5	2022.20

Cluster 3

Keyword	Links	Total link strength	Occurrences	Avg. pub. year
Nanofabrication	47	111	76	2021.67
Gold nanoparticle	99	316	59	2021.97
Nanofibre	74	254	48	2022.42
Silver nanoparticle	81	195	36	2021.97
Nanocomposite	51	98	34	2022.06
Carbon nanotube	69	139	30	2021.60
Zinc oxide nanoparticle	65	118	18	2021.94
Nanosheet	26	35	17	2022.71
Metal nanoparticle	40	74	15	2022.60
Silica nanoparticle	38	55	12	2022.33
Polyethyleneimine	47	67	10	2021.50
Poloxamer	37	53	10	2022.10
Iron oxide nanoparticle	33	46	10	2022.40
Caenorhabditis elegans	19	24	9	2022.33
Nanowire	20	24	7	2021.57
Cerium oxide nanoparticle	17	23	7	2021.71
Activated carbon	1	2	7	2021.86
Carbon nanoparticle	24	31	7	2022.00
Titanium dioxide nanoparticle	31	43	6	2021.33
Carbon tetrachloride	13	14	6	2021.83
Molecularly imprinted polymer	29	38	6	2022.17
Nanotube	12	12	6	2022.50
Nanopore	14	14	5	2020.60
Copper oxide nanoparticle	19	26	5	2021.60

Megakaryocyte	8	8	5	2021.80
Spirulina	13	16	5	2021.80

Cluster 4

Keyword	Links	Total link strength	Occurrences	Avg. pub. year
Cell encapsulation	100	274	119	2022.32
Chitosan	93	404	71	2022.20
Hyaluronic acid	101	329	69	2022.17
Gelatin	82	287	68	2022.18
Electrospinning	69	280	67	2022.18
Collagen	72	254	62	2022.03
Alginic acid	78	269	59	2022.05
Polycaprolactone	72	260	57	2021.95
Hydroxyapatite	38	78	40	2022.53
Polylactic acid	64	160	29	2021.79
Glycosaminoglycan	51	111	27	2022.07
Polyvinyl alcohol	57	147	26	2021.81
Silk	37	63	24	2021.75
Silk fibroin	35	74	23	2022.13
Phage	4	4	17	2021.94
Gelatinase a	25	33	15	2022.07
Matrix metalloproteinase	13	19	13	2021.62
Polyethylene terephthalate	44	74	11	2022.36
Titanium dioxide	16	23	10	2021.00
Silicon dioxide	15	17	10	2021.60
Silicone	22	26	9	2021.44
Dimethyl sulfoxide	3	3	9	2021.89
Edetic acid	10	12	7	2022.14
Polyethylene	22	31	6	2022.33

Cluster 5

Keyword	Links	Total link strength	Occurrences	Avg. pub. year
Electroporation	58	97	39	2022.31
Aptamer	31	40	27	2022.41

Reduced nicotinamide adenine dinucleotide	5	5	18	2021.78
Tryptophan	15	18	16	2022.38
Disulfide bond	9	11	12	2022.00
Cd68 antigen	24	29	10	2021.10
Single chain fragment variable antibody	23	25	9	2022.00
Chondroitin sulfate	30	46	9	2022.67
Methionine	6	8	8	2021.13
Oxygenase	1	1	7	2021.14
Isoflurane	5	6	7	2021.43
Immunoglobulin g1	7	11	7	2021.57
Methacrylic acid	14	18	7	2021.57
Virion	4	4	7	2022.57
Biotinylation	7	8	7	2022.71
Arabinose	11	11	6	2021.67
Schiff base	8	9	6	2021.67
Catechol	36	36	6	2021.83
Signal peptide	3	3	6	2021.83
Hyaluronidase	10	12	6	2022.00
Creatinine	9	9	6	2022.50
Streptavidin	15	16	6	2022.67
Cd40 antigen	8	9	5	2022.20
Thiol	5	5	5	2022.20

Cluster 6

Keyword	Links	Total link strength	Occurrences	Avg. pub. year
Microrna	106	266	111	2022.30
Small interfering rna	97	221	48	2022.38
Scaffold	70	145	46	2021.91
Adeno associated virus	41	68	46	2022.13
Molecularly targeted therapy	75	111	36	2022.08
Electrostimulation	36	51	29	2021.59
Viral gene delivery	21	35	26	2021.38
Neutralizing antibody	21	31	20	2021.35
Mesenchymal stem cell transplantation	20	26	18	2022.06
Magnetic nanoparticle	47	75	15	2021.87
Microsphere	36	49	15	2022.40
Hematopoietic stem cell transplantation	13	18	14	2022.57
Brain derived neurotrophic factor	21	30	11	2021.73

Keratinocyte growth factor	11	12	10	2021.70
Microrna 21	18	26	10	2023.10
Heterodimerization	7	7	6	2021.50
Autologous stem cell transplantation	6	6	6	2021.83
Fibroblast growth factor 2	7	7	5	2021.40
Bevacizumab	19	21	5	2021.60
Antibody drug conjugate	16	17	5	2022.00
Glucagon like peptide 1 receptor agonist	2	2	5	2022.20
Fucoidin	25	32	5	2023.20
Herpesviridae	7	8	5	2023.40

Cluster 7

Keyword	Links	Total link strength	Occurrences	Avg. pub. year
Liposome	94	256	62	2022.05
Photothermal therapy	65	133	31	2022.23
Lipid nanoparticle	59	103	23	2022.74
Nanoemulsion	49	85	12	2022.75
Colloid	42	45	11	2022.09
Quercetin	43	66	11	2022.09
Nanogel	56	91	11	2022.27
Lactobacillus plantarum	36	36	10	2021.80
Chitosan nanoparticle	53	94	9	2023.11
Microemulsion	42	68	8	2022.38
Mesoporous silica nanoparticle	50	88	8	2023.00
Povidone	36	49	7	2021.86
Cyclodextrin	40	63	7	2022.43
Spray drying	36	39	6	2022.33
Cell penetrating peptide	16	18	6	2023.00
Trastuzumab	40	43	6	2023.00
Liposomal delivery	41	56	5	2022.80

Cluster 8

Keyword	Links	Total link strength	Occurrences	Avg. pub. year
Macrogol	85	251	62	2022.00
Matrigel	42	73	34	2021.82
Nuclear reprogramming	42	51	29	2021.69

Spheroid cell	17	30	24	2021.63
Albumin	56	88	24	2021.83
Wnt protein	12	14	16	2021.44
Transcription factor nanog	9	12	10	2021.00
Alpha 1 antitrypsin	9	11	8	2021.75
Arginylglycylaspartic acid	15	18	8	2022.25
Notch receptor	8	8	7	2020.86
Ascorbic acid	17	17	6	2021.83
Polyacrylamide	9	10	6	2022.17

Cluster 9

Keyword	Links	Total link strength	Occurrences	Avg. pub. year
Microencapsulation	13	22	11	2022.45
Nanoencapsulation	52	83	30	2021.77
Polyacrylic acid	32	42	7	2021.57

Cluster 10

Keyword	Links	Total link strength	Occurrences	Avg. pub. year
Low density lipoprotein receptor	11	12	5	2022.20

Appendix B: protocol for translating trial phase into TRL

1. Read trial to make sure it is an application of the keyword
2. Read trial to make sure it is relevant to the specific arm of bioeng (eg tissues and medical devices)
3. Briefly read the trial and see if the technology is named
4. If it is, search for the name on Google:
    a. If it is on market TRL9
    b. If it has obtained FDA/EMA approval, TRL8
    c. If it has submitted FDA/EMA approval, TRL7

If not named, for trials with phase: (https://uhsf.nl/wp-content/uploads/2020/02/TRL_overview_UHSF_version20200206.pdf)

5. Take trial phase/status. If a double-phase ie phase 1/2, take the higher phase

a. P1 ongoing/early phase 1 complete, TRL5
b. P1 complete/P2 ongoing, TRL6
c. P2 complete/P3 ongoing, TRL7
d. P3 complete/P4 ongoing, TRL8

For trials without phase: https://www.ukri.org/wp-content/uploads/2022/01/EPSRC-11012022-Technologyreadinesslevelsfrombasicresearchtoadoptionanddiffusion.pdf

6. Read trial: search for word “safe” or “safety”
    a. If safety trial is ongoing (including recruiting and not yet recruiting), TRL5
    b. If safety trial is complete, TRL6
    c. If secondary trial ongoing (search “efficacy”), TRL6
    d. If secondary trial complete, TRL7

NB for a product already on the market for a different indication to the one on test, note this. Eg Technology X already marketed for cancer but in ongoing P2 for diabetes would be TRL9 for cancer and TRL6 for diabetes. If for comparison of two marketed products, TRL9.

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