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AI in Health Care: Powering Patient Outcomes

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The Health AI Frontier: New Opportunities for Innovation Across the Health Care Sector

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With the health care industry under pressure to improve patient outcomes while controlling costs, artificial intelligence (AI) and machine learning (ML) are quickly becoming indispensable tools. These technologies show promise in supporting decision-making, enhancing the delivery of care, and personalizing medicine. In addition, AI and ML innovations have the potential to revolutionize medical research by giving researchers access to unprecedented amounts of data that could lead to novel treatments or cures for diseases.

AI / ML in Health Care

AI and ML (which can be regarded as a branch of AI) refer to machine-driven simulations of human intelligence, with a goal of emulating the thought processes and decision-making capabilities of humans. It has potential applications in many fields, particularly health care, where it can be used to assist medical professionals with diagnostics and, more broadly, health evaluation. For example, by evaluating medical history data as well as digital imaging such as MRI scans and CT scans, machine learning algorithms are able to identify subtle anomalies that may form indicators for diseases. In addition to decision-making support, AI-powered solutions can also help health care providers deliver better care and help patients better take care of themselves. With these applications rapidly expanding in health systems worldwide, it is no surprise that these machine-simulated intelligence tools are becoming an essential resource for medical professionals. As development in these technologies continues, its use in health care will become more pervasive, allowing for a more efficient delivery of care.

Opportunities and Potential of AI in Health Care

Hospitals and medical practices are increasingly making use of AI systems to automate classification and diagnosis tasks to free up clinicians to focus on providing personalized care to their patients. AI also offers the potential to access larger data sets than ever before, helping clinicians detect patterns that would otherwise go unnoticed. This can help in uncovering novel insights into patient health, which could then be acted upon directly through targeted treatments tailored towards individual patient circumstances. In addition, AI-based medical devices such as pacemakers and insulin pumps are currently being developed to increase independence and comfort for many patients who suffer from chronic illnesses. While these benefits sometimes involve refinement and optimization of existing models, potential new opportunities for improving patient care through AI are virtually boundless.

Personalized Medicine

AI has the potential to revolutionize personalized medicine and health care outcomes, allowing society to accelerate tailored approaches for individual patients. By parsing through massive amounts of patient data, these AI systems can provide real-time insights into personalized treatments, progress tracking, and diagnoses with more accuracy than ever before. Providers further will have improved access to patient information and can use evidence-based analytics to make informed decisions more quickly, leading to the

development of personalized treatment plans as soon as a patient presents with a condition or symptom, including predictive modeling for suggested courses of action. This is an incredibly valuable tool in driving better outcomes for patients, since treatments can be personalized based on years' worth of clinical data virtually instantly. Such individualized health care can avoid adverse reactions in patients and improve outcomes in less time and at lower cost.

Better Outcomes

AI also enables more accurate diagnosis, improving patient monitoring and health outcomes, streamlining administrative processes, and creating opportunities for preventive care.

First, by applying machine learning algorithms to data from health records, health risks that might otherwise be missed can be detected, enabling life-saving interventions with early detection of diseases such as cancer. This can occur in tandem with helping physicians identify potential interactions between different drugs or treatments as well as potential medical complications.

Second, AI has the potential to drive down costs in the health care system by automating many tasks that would normally require time-intensive changes made by humans.

Third, it can reduce errors and help health care providers predict when a patient is at risk of developing certain diseases or health complications before any symptoms become apparent. All of this has the potential to help improve overall wellbeing for patients worldwide, ultimately creating better outcomes for them both physically and financially.

Drug Discovery

Drug development augmented by AI has serious potential, owing to its ability to evaluate vast amounts of data for new drug analysis and drug pathways in a short timeframe. These processes may assess visible molecular attributes representing drug combinations that were previously undiscovered, leading to highly effective treatments with fewer side effects. These treatments stemming from the use of AI can make a real difference in achieving better outcomes for patients with increased safety and accuracy.

Medical Research

On the research side, AI can be used to quickly identify patterns in large amounts of medical information. These patterns can then indicate what treatments have been effective in the past so medical professionals can use similar treatment plans for other patients with the same medical issue. When information is available faster, medical professionals are better equipped to provide more accurate diagnoses and treatments for their patients. AI also has capabilities to anticipate potential medical issues before they worsen, allowing proactive intervention before an issue becomes severe or even life-threatening. The potential benefits of AI boosting medical research yields great promise for improving outcomes for patients.

Stakeholders and Data Considerations

The use of AI in health care is rapidly increasing, and with it comes a range of personnel who are affected by its implementation. Due to the complexity of this technology there are many stakeholders involved when considering its adoption, including patients, doctors, nurses, and other medical professionals; data scientists; software developers; regulatory bodies; insurers and other payers; IT departments; as well as government organizations responsible for setting policy guidelines for health information security.

A common thread when it comes to the impact and complexity of AI systems concerns data. Data is a lifeblood of AI and ML in health care. As AI continues to become an increasingly integral part of health care, it is essential that we understand the value of data when it comes to leveraging these technologies for improved patient care. From enabling precision medicine and clinical decision support to automating mundane tasks and freeing up physicians' time – data has the potential to revolutionize how health care is delivered. It's no surprise then that a primary concern around AI in health care is data privacy. As patient data is collected from various sources such as medical records, wearable devices, or genetic testing, there is a potential for that valuable information to be exposed to malicious actors or used for unethical purposes if not properly secured. Many health care organizations have multiple databases that need to be secure from intruders, as leaks could put patients' sensitive information at risk.

Data Protection

To promote data protection, hospitals should implement strict protocols to help ensure patients' privacy rights are respected when their medical information is collected and stored. This might include measures such as secure encryption algorithms and secure storage practices in order to prevent unauthorized access or misuse of sensitive health data. Additionally, organizations should consider governance processes that ensure potential risks associated with AI technology are identified early on so they can be addressed effectively. For example, AI solutions can be deployed with appropriate certifications in order to ensure stringent standards of data protection. An effective risk-management strategy may entail regular maintenance and updating of the system in order to identify and rectify any flaws. Additionally, processes for handling data securely should be integrated into the organization's day-to-day operations in order to ensure a secure working environment for everyone involved. These efforts will help ensure that HIPAA and other relevant laws and regulations are not violated. By taking these considerations into account when adopting AI solutions, health care institutions can secure patients' private data and uphold their trust.

Data Quality

Data quality is another major consideration when integrating AI in the health care settings. The better the data, the higher the quality of predictive models and more useful the predictions from those models when being deployed. But obstacles persist: the data that is useful for AI integration may be siloed in different locations and departments, may employ different standards, and/or may be stored in computer systems that might not be interoperable. Certain otherwise useful data might even not be digitized. While more data generally provides additional benefit, the quality of that data matters. Helping stakeholders appreciate the need for quality will not only make AI solutions more useful, but it will also help them understand how to avoid pitfalls, troubleshoot when trying to determine why something didn't go according to plan, and develop action plans to make needed adjustments going forward.

Looking Forward

AI and ML offers a tremendous opportunity to revolutionize health care and drive better outcomes for patients, in part by freeing up health care professionals' time to focus on what matters most: caring for patients. Although implementing AI and ML in health care presents challenges, the challenges can be managed to ensure that AI's full potential can be realized without compromising patient safety or wellbeing. With careful planning and collaboration between stakeholders such as clinicians, hospital administrators, software developers, and regulatory bodies, health care organizations can create smarter technologies that make health care more efficient, effective, and affordable for all. An effective AI strategy and careful implementation will help health care organizations be innovative and thrive, now and into the future.

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No longer science fiction, AI and robotics are transforming healthcare, PwC.

AI in Health Care: Regulatory Landscape & Risk Mitigation

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Health care, like most industries, is grappling with the proliferation of artificial intelligence (AI) and the novel risks and benefits it presents. Balancing these risks and benefits can be especially challenging for attorneys, as the laws and regulatory regimes that may apply to a given AI technology can vary between technologies and different states and countries. Fortunately, experts from multiple institutions representing health care systems, academia, and government, through the Coalition for Health AI (CHAI), have come together and created a Blueprint which identifies and proposes solutions to issues that must be addressed in order to enable the trustworthy use of AI in health care.

Allowing AI technologies to perform tasks traditionally handled by humans presents unique risks in the health care context. The typical AI risks seen in most business contexts, such as cybersecurity risks and invisible bias in decision making, remain present. However, the risk profile in the health care context is substantially greater due to the potential of an automated decision resulting in a direct negative impact on a human's survival, causing stress, confusion, pain, suffering, or even loss of life.

Organizations operating in the health care space should conduct a holistic review of each AI technology they wish to implement to determine an overall risk profile. Areas such as ethical implications, potential for public reputation harm, degree of human oversight, potential biases, and potential regulatory concerns should be examined.

Reading the Regulatory Landscape

Rather than a uniform law governing AI technologies, certain aspects of these technologies are governed by a patchwork of laws and regulations. The resulting current regulatory framework is complex and may vary based on several factors including types of data implicated, geographic location, use case, and technical implementation. There are various efforts underway to address the regulatory gap, including the European Union's Artificial Intelligence Act (which the European Parliament recently approved) and the Blueprint for an AI Bill of Rights published by the Biden Administration in October 2022. While this shows progress toward enacting formal AI regulation, the patchwork remains.

Organizations operating in the health care space should conduct a holistic review of each AI technology they wish to implement to determine an overall risk profile.

In the absence of formal regulation, regulators and lawyers frequently look to common industry frameworks when evaluating risk, such as those published by the U.S. National Institute of Standards and Technology (NIST). Fortunately for organizations operating in the health care space, there is ample guidance and thought leadership on safely and responsibly utilizing AI technology.

In April 2023, CHAI released the first version of its Blueprint for Trustworthy AI Implementation Guidance and Assurance for Health Care. This Blueprint aligns with NIST's AI Risk Management Framework and provides a simple and informative starting point for health care organizations seeking to implement AI technologies safely and responsibly. Furthermore, the Blueprint can assist attorneys with vetting AI technologies that their clients wish to implement and in mitigating legal risk by providing a starting point for developing an objective and defensible approach for evaluating their clients' use of AI technologies.

The regulatory environment surrounding AI technologies is complex and constantly evolving. Organizations operating in the health care space should regularly review and reevaluate their use of AI technologies to ensure they are safe, ethical, beneficial to the organization, and do not violate law or industry standards.

Collusion & Competition: What Antitrust Means for AI in Health Care

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Health care companies are increasingly using artificial intelligence (AI) to create innovations, set prices, and compete with rivals. At the same time, federal and state antitrust enforcers are finding new ways to apply antitrust law to the modern, data-driven economy. Amid these myriad changes in technology and the law, the time is ripe to consider what the growth of AI in health care means for antitrust compliance.

AI and Competition

Reduced down to a word, the aim of the antitrust laws is "competition." Business practices that promote competition are generally permissible under the antitrust laws, while business practices that unreasonably restrain competition are generally forbidden. Accordingly, as AI becomes increasingly important to competition in health care, antitrust enforcement is evolving to account for novel issues posed by AI. In the context of antitrust merger reviews, for instance, antitrust enforcers are increasingly taking a broad look at how mergers might combine powerful repositories of data or market intelligence, or whether mergers might have the effect of depriving customers or competitors of the key tools or insights that they need to compete in the modern economy. In this respect, antitrust regulators are broadening their traditional regulatory playbook to scrutinize not only "horizontal" mergers (mergers between competitors), but also "vertical" mergers (mergers between a supplier and its customer). Antitrust regulators are also focused on acquisitions of "nascent" competitors, such as industry disrupters that are poised to stir the competitive pot in a given industry. As an example, if a large, established health care software provider agrees to acquire a small but promising AI startup, an antitrust regulator might review the transaction to consider whether the buyer may use the transaction to scrap a disruptive technology to protect the incumbent's existing market position or, instead, whether the transaction might be a springboard for the combined company to more broadly deploy new, innovative technology.

Reduced down to a word, the aim of the antitrust laws is "competition."

Similarly, antitrust enforcers are becoming increasingly sensitive to whether AI tools might create information asymmetries or power imbalances that could create unfair competitive advantages, whether horizontally (between competitors) or vertically (between a supplier and its customer). In these respects, companies should remember that the ultimate goal of antitrust law is for businesses to engage in full and vigorous competition on the merits. Companies therefore should not be shy about deploying AI to improve the value, quality, or accessibility of their services. But companies should also be mindful that the antitrust laws can unintentionally be violated by uses of AI that do not represent bona fide competition on the merits, such as using AI predatorily to disadvantage a rival.

> Companies therefore should not be shy about deploying AI to improve the value, quality, or accessibility of their services.

Additionally, AI can also be implicated by Section 5 of the Federal Trade Commission Act, which broadly prohibits "unfair methods of competition" and "unfair or deceptive acts of practices in or affecting commerce." For instance, the Federal Trade Commission (FTC) has recently warned businesses to "keep your AI claims in check," that is, to avoid making false or misleading statements in marketing materials about their AI technology. The FTC has also warned businesses to "be careful not to mislead consumers" with AI, such as by using AI to generate the appearance of "fake users" or so-called "doppelgängers" to interact with consumers. Unfortunately, in many contexts the line between legitimate and unfair business activity can be fact- and context-dependent, as the FTC recently made very clear in an open-ended policy statement. Therefore, these determinations can require difficult judgments by experienced antitrust counsel.

AI and Collusion

Another issue is that in certain circumstances, antitrust enforcers or private plaintiffs might claim that AI is a tool for facilitating collusion. As more and more companies adopt "algorithmic pricing" models that delegate to an AI the power to make real-time, dynamic pricing decisions, the risk arises that the companies could be alleged to be using the technology to collude. As a simple example, imagine there are four manufacturers of a particular medical device and that all four manufacturers use the same AI software to set their prices. In this situation, an antitrust enforcer could allege that the agreement to use a single pricing software amounts to price-fixing - a felony under the antitrust laws.

However, claims of algorithmic collusion could also take different forms. In a more nuanced example, imagine that the four manufacturers of a particular medical device each independently decide to use AIs to set algorithmic pricing. One week, the AIs engage in robust price competition, with each AI discounting aggressively to win more and more share. The next week, however, the AIs start to raise prices independently but in parallel with one another. The third week, one AI cuts prices drastically to try to win more business, to which the three other AIs respond in kind. The fourth week, the AIs return to raising prices in parallel with one another. Finally, the fifth week, all four AIs stabilize their prices to a level that is conspicuously higher than where prices were to begin with, and prices then remain at that above-market level for the next six months. In this example, an antitrust enforcer - or even a class-action plaintiffs' attorney - might allege that the AIs are engaging in "algorithmic collusion."

It remains to be seen how antitrust enforcers and courts will determine whether criminal or even civil liability can apply for algorithmic collusion. Until then, companies should become attuned to these risks and consider monitoring their algorithmic pricing tools on an ongoing basis to detect and prevent against situations that could raise even the appearance of improper coordination.

Standards-Setting and AI

One last area of antitrust sensitivity for AI in health care is the role of standards-setting. Standards-setting is a frequent area of antitrust sensitivity, in that it brings together separate companies, potentially including competitors, to agree upon a single set of technological or operational practices for the industry to adopt as the single governing "standard." To be clear, standards-setting is not inherently problematic under the antitrust laws. To the contrary, when done correctly standards-setting can be highly pro-competitive by creating efficiencies that lessen costs and create a more level playing field for all players to compete. When done wrongly, however, standards-setting can not only raise issues of collusion between competitors but also give the standard-bearer an effective monopoly over an entire industry.

Antitrust will play a central role in AI-related standards-setting. For instance, industry coalitions might emerge proposing standards, rules of ethics, or informal "best practices" on important issues like AI data security, on what sorts of disclosures are made to patients about the use of AI, or on lessening the risks of bias in AI. The adoption of these sorts of standards may create important, potentially life-saving, benefits for the industry and society at large. But in doing so, companies will need to keep antitrust compliance top-of-mind. Antitrust enforcers will look skeptically at any standards, rules of ethics, or best practices that have the effect of foreclosing rivals or potential disruptors from fully competing on the merits. Similarly, antitrust enforcers may take issue with any standards that set unreasonably low bars for competitors to follow. For instance, if a group of hospital systems adopted an industry "best practice" that has the effect of denying patients meaningful choices about their doctors' use of AI, then the adoption of such a practice could be deemed an improper restraint of trade in violation of the antitrust laws.

Looking Forward

AI is poised to unlock tremendous insights, innovation, and value in the health care industry. As these changes unfold, companies will need to ensure that their AI practices comply with the antitrust laws. Companies should be mindful to ensure that their AI practices do not unreasonably foreclose rivals, create unfair or coercive power asymmetries, facilitate collusion, or lead to unreasonably low standards of competition. Instead, companies should use AI to sharpen their competitive edge, enhance the value of their services, or better respond to supply and demand conditions. By using AI to compete on the merits, companies will stay compliant with the antitrust laws.

Biden Executive Order on AI Oversight, Development, and Use: Implications for the Health Care Industry

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On Monday, October 30, President Biden signed an executive order (EO) aimed at overhauling the governance and oversight of artificial intelligence (AI) and technological infrastructure, including setting standards for AI used in the health care industry. The order seeks to strengthen privacy-preserving research and technologies, while developing guidelines for federal agencies. The provisions in this order will have a lasting impact on all facets of the health care industry that utilize or may in the future utilize AI models and systems.

Prior to the release of the EO, the administration met with various stakeholders, including lawmakers, leaders in computer science, civil rights, law, and the business community. Additionally, conversations occurred with leading AI companies to help ensure that the private sector will commit to the principles laid out by the administration. Dubbed a "Blueprint for an AI Bill of Rights," the administration intends to continue coordinating future actions with domestic stakeholders, with the hope that it serves as a model for international action moving forward. Meanwhile, Congress is expected to develop legislation at some point on AI oversight.

Specific to health care, this broad, 63-page order seeks to:

- Protect Americans' Privacy by establishing an **AI Task Force**.
  - The Department of Health and Human Services (HHS) and the Secretary of Veterans Affairs (The VA) will establish an AI Task Force that will develop policies and frameworks, possibly including regulatory action, for use of AI in health sector, including drug and device safety; public health; health care delivery, etc.
- Stand Up for Consumers, Patients, and Students by developing **Personalized Immune-Response Profiles for Patients under the leadership of HHS**.
- Create **standards for development of AI synthetic materials** and protect against AI synthesis of dangerous biological materials.
  - The EO directs the Secretary of HHS and several other heads of agencies to establish a framework within 180 days of October 30, 2023, to, "Encourage providers of synthetic nucleic acid sequences to implement comprehensive, scalable, and verifiable synthetic nucleic acid procurement screening mechanisms, including standards and recommended incentives." This effort will include engaging with industry and relevant stakeholders to establish a safe path forward with synthetic DNA.
  - Establish **a new safety program** through HHS to receive reports of harms or unsafe health care practices involving AI and work to remedy them.
  - Under the leadership of the VA, advance systems that will improve the **quality of veterans' health care** hosting two three-month AI Tech Sprint competitions.

  - **Ensure quicker grant processes** by speeding up the process for awarding grants for National Institute of Health Artificial Intelligence/ Machine Learning Consortium to Advance Health Equity and Research Diversity (AIM-AHEAD) activities in underserved communities.

- Support workers by **developing a key set of standards and publishing a report forecasting potential labor-market impacts of AI**.
- Promote Innovation and Competition.
  - **Pilot the National AI Research Resource** in order to provide researchers and students access to AI resources and data.
  - **Expand grant opportunities for AI research in health care by** allocating the 2024 Leading Edge Acceleration Project and prioritizing initiatives that will improve health care data to support development of AI tools for clinical care, population health, public health, etc.
- Advance American Leadership Abroad by accelerating the development and implementation of AI standards internationally, ensuring AI is universally interoperable and promoting the development and deployment of AI abroad to solve global challenges and dangers to infrastructure.
- Ensure Responsible and Effective Government Use of AI by **issuing guidance** for agency use of AI and **hiring** AI professionals in the government.

Notably, the EO has bicameral, bipartisan support on Capitol Hill. House Energy and Commerce Committee Chair, Cathy McMorris Rodgers (R-WA), said of the order:

"As companies begin to incorporate AI, we need to protect and secure the personal information of every American, especially our children, while preserving innovation in the process. I agree with President Biden that the best way to do this is by enacting a comprehensive data privacy and security law, which should be the first step towards cementing America's leadership in AI."

Senate Commerce Chair, Maria Cantwell (D-WA), said of the order,

"[Biden's] Executive Order creates a new safety institute at the Commerce Department to set standards for third-party testing; identifies ways to strengthen federal support for workers; develops training and technical assistance to fight algorithmic discrimination and acts to combat deepfakes. The President's leadership at the G7 resulted in the important adoption of AI principles and a code of conduct for companies. As we move forward, Congress must act on legislation to set a permanent framework for the development and deployment of AI."

This sweeping EO marks the first significant step taken by the federal government to ensure critical protocols are in place to protect American's safety and privacy in the new world of AI. The private sector, which has contemplated a future heavily reliant upon AI for many years, is expected to play an important role going forward as the federal orders take shape.

FDA's Guidance Proposes Flexible Use of AI in Medical Devices

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On April 3, 2023, U.S. Food and Drug Administration (FDA) issued its much anticipated draft guidance, "Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions" (Draft Guidance).

While FDA has already approved, authorized, or cleared over 500 AI/ML devices, FDA continues to receive an increasing number of marketing submissions and pre-submissions for AI/ML-enabled medical devices. FDA's traditional approach for the regulation of hardware-based medical devices, however, is not well suited for the faster, iterative design and development, and type of validation used for software device functions, including Software as a Medical Device.

The benefit of AI/ML is that it can optimize performance over time and continuously learn based on real world experience. Under the traditional FDA regulatory framework, changes to software require new risk assessments to determine whether the change affects the functionality or risk category before releasing each change. That is, the algorithm is essentially locked and cannot change while out in the market, defeating the optimization of AI/ML technology.

To address this issue, FDA outlined a Predetermined Change Control Plan for premarket submissions in its 2019 Discussion Paper and 2021 AI/ML-based Software as a Medical Device Action Plan, allowing manufacturers to predict algorithm changes and implement future modifications without requiring additional marketing submissions.

Under a Predetermined Change Control Plan, manufacturers would be required to submit:

1. a detailed description of the specific, planned device modifications;
2. the methodology to develop, validate, and implement these modifications in a manner that ensures the continued safety and effectiveness of the devices; and
3. an impact assessment to assess the benefits and risks of the planned modifications and risk mitigations.

The Draft Guidance builds on the proposed framework and helps clarify the types of modifications that should be included in the Predetermined Change Control Plan. Notably, FDA also proposes that the Predetermined Change Control Plan articulated in the initial proposed framework be used for not only AI/ML-enabled Software as a Medical Device, but for all AI/ML-enabled device software functions, including software functions that are part of or control hardware medical devices.

Under this framework, FDA expects manufacturers to commit to transparency and real-world performance monitoring, and to periodically update FDA on changes implemented as part of the approved pre-specifications and algorithm change protocol. In addition, modifications should be implemented following appropriate, well-defined practices, such as the Good Machine Learning Practice guiding principles jointly

developed by FDA, Health Canada, and the United Kingdom's Medicines and Healthcare products Regulatory Agency.

Ultimately, the new Draft Guidance seeks to enable manufacturers to market medical devices with continuously learning algorithms without having to obtain a new authorization or clearance for each change, so long as the changes are in line with the predetermined plan. Through this Draft Guidance, FDA seeks to provide flexibility for devices with continuously learning algorithms, while retaining certain limits on the software to safeguard continued safety and effectiveness of the devices.

Under the traditional FDA regulatory framework, changes to software require new risk assessments to determine whether the change affects the functionality or risk category before releasing each change.

The Role of AI in Health Care M&A: Driving Value in a Difficult Market

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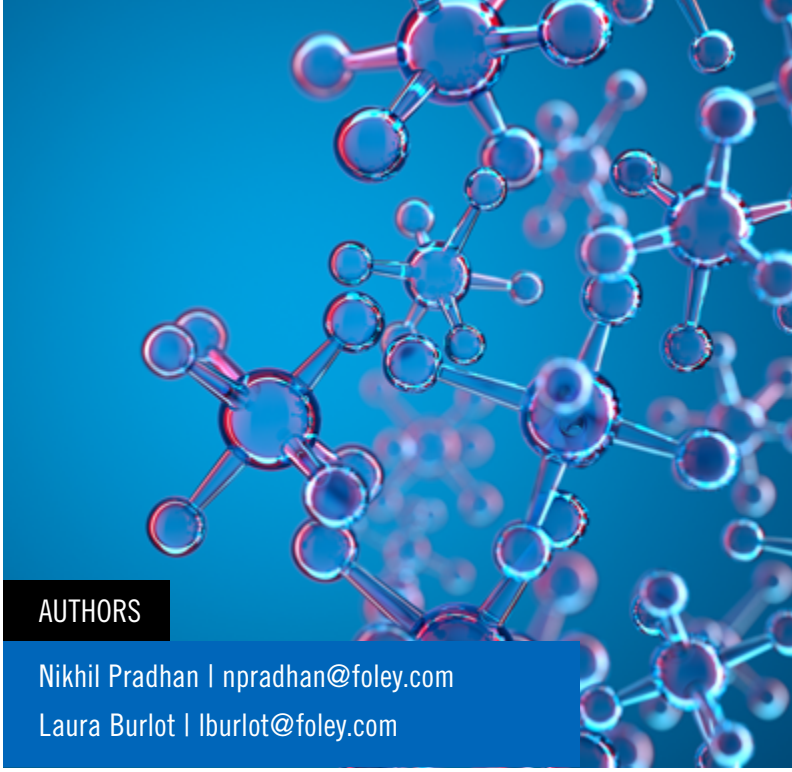

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Health care merger and acquisition (M&A) activity reached a significant level in 2022, even if not matching 2021's record-breaking standard. This reflects the overall economy's holding pattern in which resources are still being deployed strategically, but not at full throttle. At the same time, prognosticators including Moody's have predicted that dealmaking may remain high over the next 12 to 18 months. This is due to a combination of factors, including pharmaceutical companies seeking to restock their pipelines in the face of approaching patent cliffs and long-term pricing pressure.

Many of last year's deals were underscored by significant ties to artificial intelligence (AI) technologies, a trend likely to become more prevalent going forward. More broadly, Precedence Research estimated that the global AI in health care market will grow to over US$180 billion by 2030 - up from a 2022 estimate of US$15 billion.

In particular, AI technologies can drive value for health care companies by:

- Adding new or complementary capabilities
- Expanding customer and user bases
- Enabling firms to extract new insights from existing data
- Allowing access to new data sources

This article will review several health care M&A deals from 2022 and Q1 2023 to draw out these trends and highlight how companies can acquire AI capabilities to succeed in the rapidly evolving health care landscape.

Notable Health Care AI Deals

Many of the top 10 medical tech M&A deals in 2022, as identified by Fierce Biotech, had direct AI considerations. For example, Microsoft's acquisition of Nuance was based on expanding the addressable market for its Microsoft Cloud for Health Care platform:

"In shelling out the big bucks, Microsoft forecasted that adding Nuance's conversational AI and other ambient intelligence products specifically to its Microsoft Cloud for Health Care service would double its total addressable market among health care providers, creating a revenue opportunity of up to US$500 billion. The duo, which have been working together since 2019, aims to help reduce clinicians' workloads — and therefore the epidemic of health care worker burnout — by embedding automated note-taking technology and other cloud-based tools into electronic health record software."

Meanwhile, R1 RCM's purchase of Cloudmed was directed towards adding data processing capabilities to uncover added revenue streams:

"It kicked off 2022 by offering US$4.1 billion in stock to purchase Atlanta-based Cloudmed, which has built an AI-powered, cloud-based platform that hospitals and health systems can use to analyze medical records and billing and insurance data, with an aim of uncovering "underpaid or unidentified revenue."

While most AI activity in the pharmaceutical and drug development space has focused on venture capital investments, BioNTech made a notable acquisition of InstaDeep to add InstaDeep's AI technologies for drug discovery and manufacturing.

In addition, several other top 10 deals had AI-related nuances, particularly in generating new data streams and other integrations. The QuidelOrtho merger combined Quidel's digital health platforms with Ortho's point of care solutions, while Stryker's acquisition of Vocera blends voice assistance with day-to-day clinical communication data.

These major deals illustrate some of the value propositions of AI technology, namely in terms of how they demonstrate one or more of the ways in which AI can value.

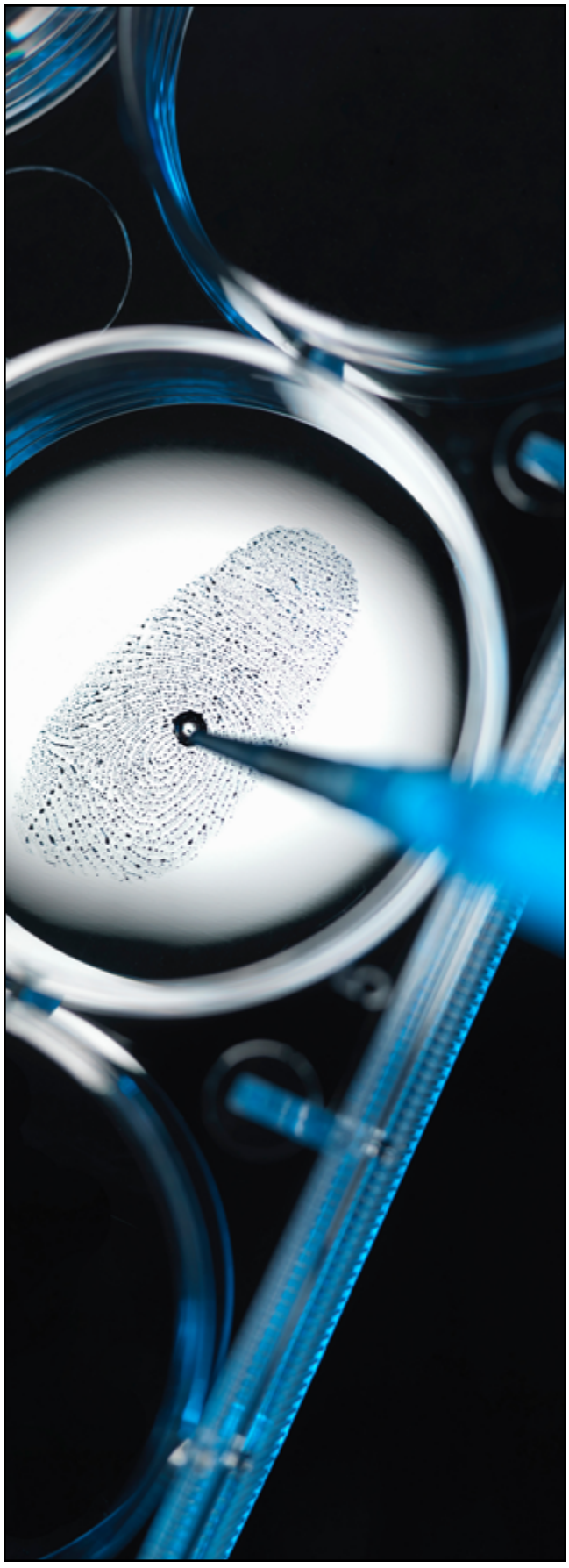
Many of last year's deals were underscored by significant ties to artificial intelligence (AI) technologies, a trend likely to become more prevalent going forward.

AI Value Propositions in 2022/2023 M&A Deals

M&A Event	Deal Size	New or Complementary Capabilities	Expanded Customer or User Base	Extract Insights from Existing Data	Access to New Data Sources
Microsoft & Nuance	US$19.7bn	✓	✓		
R1 RCM & Cloudmed	US$4.1bn			✓	
BD & Parata	US$1.5bn		✓		
Quidel & Ortho	US$6bn	✓	✓		✓
Stryker & Vocera	US$3.1bn	✓			✓
BioNTech & InstaDeep	US$700m	✓		✓	
GE HealthCare & Caption Health	N/A	✓			
Healthful & Sympto Health	N/A	✓			

Further Insights and 2023 Outlook

These trends are also consistent with 2022's M&A activity for hospital and health systems. Commentators have noted that activity in this space underscores that "the movement to capability-based scale is much more prominent than adjacent market-based scale," particularly in cross-market mergers that create value without changing "the competitive structure of the markets involved in the merger — there is no increase in the concentration of local hospitals or health systems, an increasingly important feature considering the current regulatory landscape." A noteworthy element of many of this year's cross-market mergers is that the systems have a common focus (e.g., rural health), complementary skillsets (e.g., academic medicine and community health), or a shared desire to improve health outcomes. These common focuses – including emphasis on complementary skillsets – reflect the value proposition of acquiring AI businesses to reach existing customers in new ways, enter new markets, expand market share, and create new value for customers.



2023's early M&A activity demonstrates how AI plays can add value for health care companies through all four key value propositions. On the medical device side, in its first acquisition as a sole company, GE HealthCare is bolstering its ultrasound portfolio by acquiring Caption Health's AI-powered technology for helping guide medical workers through ultrasound procedures. Following its acquisition of Nuance, noted above, Microsoft further recently announced a new collaboration with Epic to integrate their platforms for boosting productivity and improving patient care. Inflect Health – the incubator of Vituity – merged its startup Healthful with Sympto Health, combining each company's core technologies to create a new AI and personalized care automation platform.

Pharmaceutical companies with long-term outlooks may also be looking for strategies to compete after the patent landscape changes by around 2030 for several blockbuster drugs. Companies developing computational drug discovery technologies may prove to be valuable acquisition targets, providing useful platforms to plug into existing drug development roadmaps.

What's Ahead?

Adding AI capabilities through M&A can help health care companies innovate and create value in several different ways. Recent deals in this space have emphasized how AI solutions can create new patient service opportunities, whether companies have more traditional business and care models or are more technology-centric. These trends are expected to continue as the AI in health care market expands into the US$100 billion-plus range in the coming years. From health care systems seeking to add data analytics and patient-service capabilities, to medical device companies looking to improve how their technologies operate and deliver the right results at the right time, to pharmaceutical companies needing to strategize in view of impending patent cliffs, acquiring AI technologies will be valuable for continued success.

Key Contractual Considerations for Health AI and Hospital Collaborations

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If artificial intelligence (AI) is the vehicle that will revolutionize health care, data is the fuel that will propel the revolution. Health AI startups have recognized an unprecedented opportunity to create a transformative network effect, akin to many data companies, by collaborating with health systems and hospitals.

The idea is simple yet powerful: by partnering with the hospitals, health AI startups can access vast amounts of data, which when aggregated and analyzed, can generate more refined products, greater efficiencies and cost savings, and meaningful impacts to problems that have plagued the health care ecosystem for decades. These products can not only optimize patient care and hospital operations but also become invaluable assets to other stakeholders like pharmaceutical and medical device companies.

For hospitals, the proposition is tempting. By sharing their data, they get access to cutting-edge AI solutions that promise to cut costs, enhance patient and provider experiences, and drive revenue. Meanwhile, for AI startups, the continual flow of data means more refined algorithms, more accurate predictions, and an expanding portfolio of insights.

However, the dynamics of these partnerships are not straightforward. When health AI startups and hospitals sit at the negotiation table, both sides must consider several key topics:

Data Use Rights

Many health AI startups are blindsided when learning how the Health Insurance Portability and Accountability Act (HIPAA) and state privacy laws limit data use. Absent certain authorizations from patients or rights appropriately granted to the startup by the hospital, HIPAA and other regulations can create barriers for service providers, like an AI startup, to perform activities outside of an agreement's defined services that use patient data. Necessary product-development activities, not considered part of the defined services provided to the hospital-client, like machine learning and using patient data to create training data, are limited if not carefully negotiated.

To hospitals, protecting patient data is paramount due to regulatory, ethical, and reputational concerns.

Data Protection

To hospitals, protecting patient data is paramount due to regulatory, ethical, and reputational concerns, as well as an acute and ever-growing understanding of the true value of their patient data. Hospitals tend to prefer non-exclusive rights, ensuring the flexibility to use competing AI tools or share data with other entities as needed. Startups may seek flexibility through the use of de-identified patient data and the ability to license the de-identified data through a fully paid, perpetual and non-revocable license grant, which helps to ensure that they can utilize the data indefinitely, as their algorithms evolve.

Pricing Strategy

Hospitals will want to ensure the AI solution offers a clear and justifiable return on investment. Startups will aim to get a foot in the door. Common pricing strategies include low or no-cost trial or pilot terms in exchange for valuable data insights and collaboration clauses requiring both parties to routinely meet and share insights gleaned from the data and the AI solution's performance. For startups seeking to evidence value and predictable revenue, opting for a pricing strategy that includes subscription-based pricing can serve multiple purposes, including steady cash flow, recurring revenue, and enhancing attractiveness to potential investors and customers.

Term Length

Hospitals may prefer shorter-term contracts initially to test the efficiency and reliability of the AI solution without a lengthy commitment. They might also negotiate conditions where they can exit the contract should the tool not meet specified performance metrics. From the startup's perspective, stability and predictability are vital especially for future acquisition or fundraising purposes. They'd want longer-term contracts, offering them revenue consistency. To entice hospitals into these, startups might offer discounted prices for longer commitments. Discounts (and other pricing strategies and contract terms) should always be considered for potential fraud and abuse implications inasmuch as hospitals are likely participants in the Federal Health Care Programs including Medicare and Medicaid.

Regulatory Requirements

Some AI software may be regulated by the U.S. Food and Drug Administration (FDA) as Software as a Medical Device (SaMD) depending on how the software operates and what claims are made. Hospitals will likely look to the AI startup to provide representations and warranties that the software is compliant with laws and some may require that the company has performed a regulatory determination of whether the product is subject to FDA requirements as a medical device. This can be challenging for AI products that may undergo regular changes and adaptations.

Post-Termination Data Handling

Once the contract ends, hospitals should seek assurances that patient data is either returned or destroyed securely. They would seek clear clauses that prohibit any further use of their data, ensuring patient confidentiality and compliance with regulations. On the other hand, AI startups might negotiate terms that allow them to retain derivative data (insights drawn from the raw data) or de-identified datasets, aiding in further refining their algorithms long after the termination of the relationship between the hospital and the AI startup.

Renewal Rights

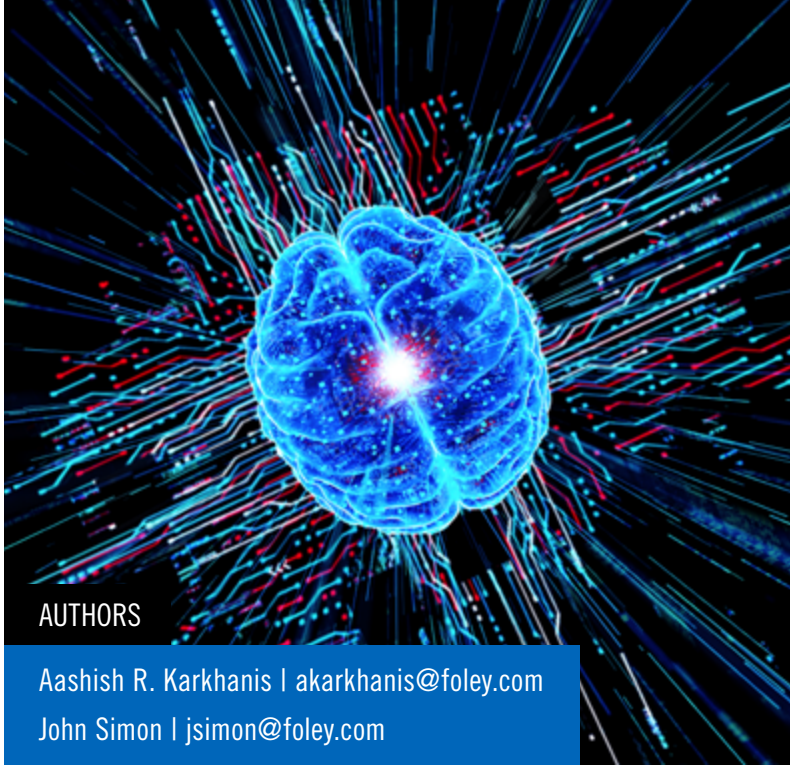
As the contract term nears completion, hospitals may prefer manual renewals, giving them an opportunity to reassess the AI system's performance and renegotiate contractual terms if needed. They would want clear notice periods to avoid automatic renewals without their explicit consent. Conversely, AI startups tend to favor automatic renewals, seeing them as a conduit to sustained revenue. They'd aim for clauses that default to automatic renewal unless the hospital explicitly opts out.

Change of Control Provisions

In the event of a takeover or change in the AI startup's ownership, what happens to the contract? Is there a need for prior notice or approval? In the event that a change in control provision is triggered, the hospital would want assurances about data handling and solution continuity. They might require prior notice or even an option to terminate the contract in such events. That said, startups might resist overly restrictive notice or consent provisions which could deter potential investors or acquirers. As such, they'd negotiate for reasonable notice periods and clauses that are not too prohibitive to accommodate flexibility during mergers or takeovers.

AI has the ability to bring immeasurable and seismic change to the health care industry. Health systems, hospitals, and startups are well-positioned to drive innovation through thoughtful and meaningful partnerships. As the partnerships deepen, it's imperative for all parties to have clear, forward-looking agreements that safeguard interests, respect data privacy, and continue to push the boundaries of what AI can achieve in health care.

Building Biotech with Brains: Strategies for Maximizing Value of AI-Driven Biotechnology Inventions



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The rapid rise of artificial intelligence (AI) and machine learning (ML) in biotechnology products and services is becoming a driver of the personalized medicine and health care sectors. While this integration can require special consideration during development of a patent portfolio, stakeholders across engineering, legal, and executive teams in both established companies and start-ups can leverage it to create valuable intellectual property (IP) assets in the marketplace. Technology and legal teams in particular can work together to develop stronger IP that applies machine learning applications to biotechnology, with an R&D process and marketplace analysis that is aware of its unique IP pressure points.

Identifying the Nexus Between Biotechnology & AI/ML

When building a robust patent portfolio and broadly capturing potential IP assets, stakeholders should approach the convergence of high-tech/biotechnology holistically. That is, IP managers should consider all potential implementations of the integrated ML/biotech asset in order to build out and cover the technical objectives underlying the commercial embodiments. Although inventors may focus on any one particular embodiment, IP portfolio managers should analyze assets from a wider lens. While this may be true across the technical spectrum, the holistic viewpoint becomes particularly important on the frontier of new technologies involving both high-tech and biotechnology components.

Product development processes can capture important IP insights early with targeted inquiries about the technology itself. Consider whether there are multiple potential data inputs that could yield a useful output metric. For instance, a particular metric for a disease could be evaluated based on the presence of particular genetic markers or by the accumulation of misfolded proteins. Generally, all data sets capable of yielding an objective metric when integrated into the machine learning model could be the basis for valuable IP.

Processes and models to analyze potentially unique data can also yield strong IP. If an asset relies on a process for obtaining unique data that enables you to train a model faster and with more accuracy, focusing various patents on generation and management of the data can protect from a competitor that gains access to similar data in the future.

Navigating prohibitions on patenting abstract ideas under the *Alice* framework can be critical when the platform is based on improvements to the ML/AI models themselves. Courts have consistently interpreted *Alice* to favor claims focused on improvements to the tangible concepts and disfavored claims directed solely to algorithms. Companies should focus on how the technology gathers or integrates the raw data, as well as novel physical elements that result in technical improvements to any process or product. This should extend beyond the preferred commercial embodiments that will be covered by your claims.

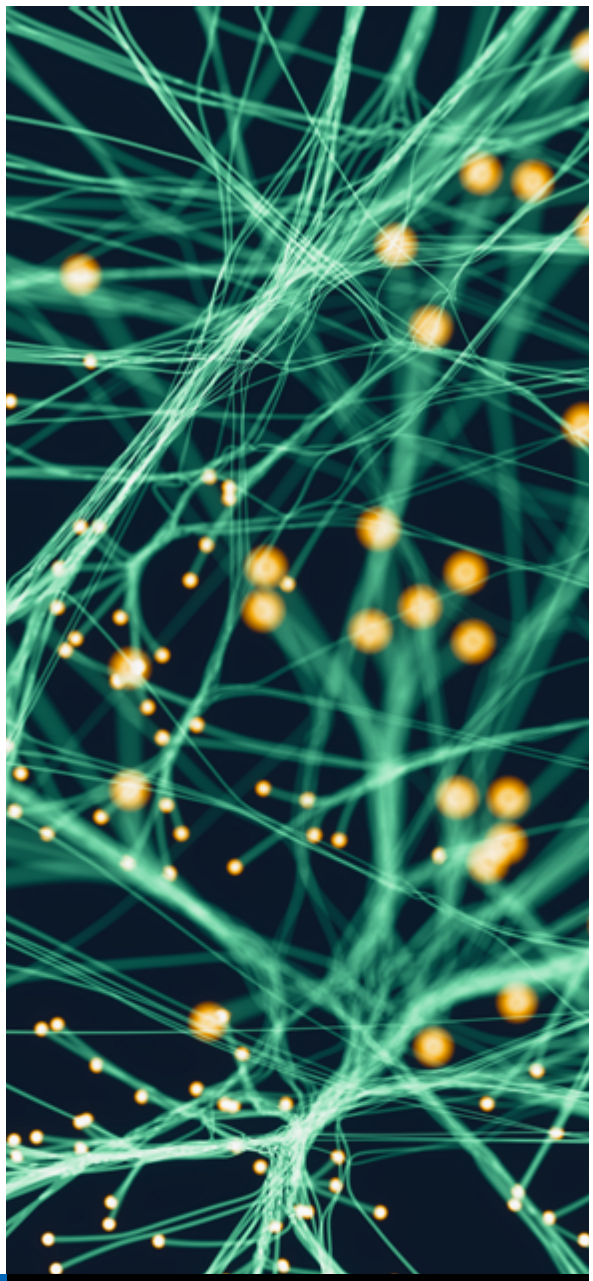
Building a Patent Portfolio for AI-Driven Biotech that Maximizes Competitive Advantage

Whether a business is primarily focused on the AI components or the biotechnology components can inform its strategic direction for creating impactful patent assets. For example, many pharmaceutical companies center their IP assets on the products and methods yielded as a result of using an AI/ML model, while in contrast many biotechnology startups base their business platform on particular ML models and data driving those models rather than on any one particular output. Further, companies interested in drug discovery or novel therapeutics may utilize their ML or AI asset as an analytical tool for converting raw data into a useful metric for disease or a new drug candidate. In this case, there may be multiple machine learning models capable of producing a therapeutically or diagnostically useful metric based on the raw data.

Each of these strategic directions can require distinct technical and legal analyses:

- Where the output data provides a useful metric – for example, the likelihood of successful treatment or novel drug candidates – companies may want to devote resources to protecting the specific output delivered using the AI solution as opposed to the AI solution itself.
- When the business focus is on the particular output generated, providing as many models and examples as possible in a patent application can maximize value.
- Where the AI solution can be applied to a broad range of actions and insights, the IP focus should be on the model and data input. Examples might include advanced ML systems capable of analyzing and finding patterns in genes or biomarkers indicating the presence of a disease and/or likelihood of successful treatment.

Ultimately, the strategic direction and R&D processes for developing high-value and impact IP for AI-driven biotechnology can be informed by the positioning of the company in the market and specific features of company products and services at the nexus between AI and biotechnology.



When building a robust patent portfolio and broadly capturing potential IP assets, stakeholders should approach the convergence of high-tech/biotechnology holistically.

IP Toolbox Is Crucial In AI-Powered Drug Discovery

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Navigating the complex landscape of drug discovery requires innovative strategies and interdisciplinary collaborations spanning biotechnology, pharmacology, medicine and engineering.

As the cost of developing new drugs surges, the pharmaceutical industry is increasingly driven to explore the potential of artificial intelligence and machine learning technologies to reshape research, expedite timelines and curtail costs.

Yet, amid this promising innovation lie potential intellectual property pitfalls due to the industry's robust reliance on proprietary drug revenue.

Use of Artificial Intelligence/Machine Learning in Drug Discovery

Escalating research and development costs, predicted to rise from approximately $1 billion to over $2 billion, are spurring interest in AI and machine learning technologies as transformative tools to streamline drug discovery, enhance patient outcomes and drive down costs.

Some key AI and machine learning applications in this sphere include predictive modeling, image analysis and pattern recognition, virtual screening and data analysis, personalized medicine, and ability to gain new insights.

Predictive Modeling

AI and machine learning can be used to build predictive models to facilitate the identification of promising drug candidates for targeted diseases, prioritizing molecules and compounds for further investigation.

Image Analysis and Pattern Recognition

AI and machine learning can be used to analyze images of cells and tissues to identify patterns and features, providing insights into disease interactions and drug efficacy.

Virtual Screening and Data Analysis

AI and machine learning can be used to analyze large and complex data sets to inform potential uses for existing drugs in treating other diseases or pinpoint diseases that may be effectively treated with novel drugs.

Personalized Medicine

Similar to traditional data analysis, AI and machine learning can analyze patient data on a much larger scale to identify specific patient populations that may benefit from a particular drug. It can also be used to reduce medical errors, detect diseases earlier, provide personalized treatment plans, improve self-care and reduce medical costs, among other benefits to improve patient outcomes.

Gaining New Insights

AI and machine learning can be used to perform various downstream biomedical tasks, generating invaluable insights for drug discovery and research. For example, Microsoft Corp.'s BioGPT tool — trained on a vast pool of biomedical research — can answer queries, classify documents, extract data and more.

Understanding the IP Toolbox for Drug Discovery Companies and How It Intersects With AI and Machine Learning

IP protection serves as a vital buffer for drug discovery companies, safeguarding investments and technology while fueling a competitive edge. Below are key IP tools for drug discovery:

Data Protection

Data serves as a pivotal asset in drug discovery, providing exclusive access to unique insights that can expedite drug discovery and development, bolstering a company's competitive edge.

Accordingly, data can serve as one of the most important, if not the most important asset, a drug discovery company has. Having proprietary data allows companies to perform nuanced analysis, identifying promising drug candidates faster and with higher precision, thereby reducing costs and accelerating time-to-market.

Data exclusivity also carries significant weight. It offers companies a defined period of time to utilize and profit from their data without interference or obligations to others. Defined data protection strategies that give the drug discovery company control over the use and access of its proprietary data ensures that this valuable asset remains secure, maintaining its value and the company's competitive advantage.

Patents

Patents are critical for drug discovery companies.

They can cover new drugs, formulations, compounds, molecules and methods of treatment. They can also protect innovations in data analysis and visualization techniques using AI and machine learning training, applications of AI and machine learning models, and processes for various aspects of drug development, design, and target identification.

Patents further provide companies an exclusive right to exclude others from making, using or selling their innovations for a limited period, typically 20 years from the patent application filing date. Patent filings related to AI and machine learning in drug discovery have been steadily growing.

This trend suggests that patents are likely to play an increasingly important role in not only the development and monetization of new drugs in the future, but also for collaborations and negotiations between drug discovery companies and large pharmaceutical companies.

Trade Secrets

Not all types of innovation are suitable for patenting. In addition to patents, trade secrets can protect valuable information generally not known to the public that provides a competitive advantage or economic benefit from being secret.

IP protection serves as a vital buffer for drug discovery companies, safeguarding investments and technology while fueling a competitive edge.

In the context of AI and machine learning and drug discovery, such information can include training data for AI and machine learning models, software code, data analysis processes, and other types of confidential information related to drug development or analysis processes. Companies relying on trade secrets can consider having robust protection protocols in place that are periodically reviewed and reinforced to maintain secrecy.

However, there is no recourse if a competitor independently develops the same technology.

Copyrights

Drug discovery companies can use copyrights to protect original works, such as scientific publications, marketing materials, training materials and software code — thus preventing unauthorized use or replication and ensuring exclusive rights to profit from these works.

Trademarks

Trademarks can play an important role in a drug discovery company's success, even though their direct impact on the science of drug discovery might not be obvious.

For instance, trademarks establish a unique identity for a company's product in a crowded marketplace and can be used to establish trust and build goodwill, assuring customers about the efficacy, safety and reliability of any new drugs developed using a company's trademarked drug discovery platform.

Licensing Agreements

Drug discovery companies may enter into IP-related agreements with other parties. These include joint development agreements, data sharing licenses, patent license agreements, technology license agreements, among others. Such agreements may allow drug discovery companies to generate revenue and collaborate with other companies or researchers while protecting their own IP.

IP Considerations in Data Sharing Between Drug Discovery Companies and Large Pharmaceutical Companies

AI and machine learning models require large data sets that may be owned, developed and/or shared by multiple entities. Two example scenarios may be:

Scenario 1: A drug discovery company receives a list of compounds or molecules from a large pharmaceutical company to identify other diseases that those compounds or molecules may be used to effectively treat.

Scenario 2: A drug discovery company receives a list of genes, classifiers, biomarkers, or other indicators associated with a particular disease to identify new compounds or molecules that may be leveraged for treatment.

In both scenarios, a drug discovery company needs to be able to safeguard — via appropriate licensing agreements — its significant investment in developing, maintaining and using AI and machine learning models. They also want to maintain a competitive advantage, prevent misuse, negotiate favorable monetary/royalty benchmarks, and ensure compliance with regulatory requirements.

Some issues to consider when drafting such an agreement include data ownership, use, protection, exclusivity, and quality, regulatory compliance and IP.

Data Ownership

Clear definitions of who owns what are highly recommended in the agreement.

Ownership considerations may be complicated if third-party data is involved, if data from multiple sources is combined to create new data sets, or if raw data is pre-processed or post-processed.

For AI and machine learning applications, companies can define boundaries on who owns outputs and insights from the model, as well as any training data utilized. In general, data ownership rights can consider the current data owners, the types of data, the sources of data and how data is used.

Data Use and Protection

Like data ownership, companies can consider defining the purpose and scope of data use in the agreement to avoid misuse or unintended consequences.

Data use clauses can define how data can be used, for what purpose and by whom. Data protection is an important aspect for data sharing. Parties can have policies, protocols and protections in place to safeguard data, including data encryption, secure and authenticated storage, data back-up and replication, and limited access.

A clear understanding of how the data is kept confidential, including how it is shared, stored and protected from unauthorized access or disclosure is desirable.

Data Exclusivity

A drug discovery company may desire exclusive access to the data for a period of time, allowing them to use the data for research purposes without interference from, or obligations to, other parties.

As AI and machine learning models are updated or new models are generated, in addition to data ownership, use, and protection issues, the agreement can clearly define data exclusivity clauses and have provisions to prevent the circumvention of the data exclusivity clauses.

Data Quality

The quality and format of the data received — and the data provided — between the drug discovery company and the pharmaceutical partner can be negotiated and agreed upon in advance to ensure suitability of the data for the intended purpose.

Regulatory Compliance

Data sharing may also be subject to regulatory requirements, such as data privacy regulations, U.S. Food and Drug Administration regulations, and the Health Insurance Portability and Accountability Act. Compliance with these requirements can be carefully considered and addressed in the agreement.

Patents

The agreement can clearly identify any patents that may be affected by data sharing and their ownership.

Necessary licenses or permissions must be obtained to avoid unintended patent infringement issues. The drug discovery company should have a clear understanding of the patents they own and the rights they have to license them to a pharmaceutical partner, as well as the legal risks and exposure associated with infringement of patent rights.

Joint IP

The drug discovery company and pharmaceutical partner can negotiate patent ownership, cost sharing, litigation and legal liability associated with patenting new technology developed as a result of data sharing or joint development.

For example, who decides what to patent, who controls prosecution, who bears the cost of prosecution, and who controls litigation resulting from the patents can all be clearly specified in the agreement. This can avoid surprises and confusion where a party decides to file a patent individually without the other party's knowledge.

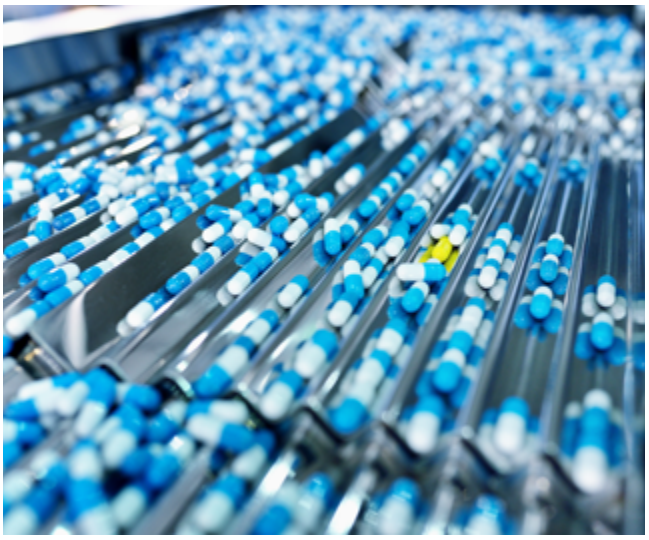
Three Key Issues to Consider

Finally, licensing agreements between drug discovery companies and large pharmaceutical companies involve a range of intellectual property considerations that need to be carefully considered, understood, and addressed to protect the interests of both parties.

Here are the top 3 issues that drug discovery companies can keep in mind:

1. Clearly define ownership, use, exclusivity and protection of AI and machine learning models and the data used.
2. Preserve monetary or royalty rights from any downstream updates to, or development of new, AI and machine learning models, as well as freedom to use AI and machine learning models.
3. Carefully consider implications of IP jointly developed.

As drug discovery companies embark on collaborations with large pharmaceutical companies, astute IP management has never been more crucial.



The accelerating integration of AI and machine learning technologies in drug discovery presents both unprecedented opportunities for innovation and unique challenges to intellectual property rights. As the value of data rises, these companies need to pay scrupulous attention to their IP assets to ensure their rights are adequately protected, their proprietary technologies are secured, and their competitive edge is maintained.

A harmonious balance between open collaboration and strategic protection of IP assets is vital. Companies should foster relationships underpinned by transparent and mutually beneficial IP licensing agreements, ensuring that ownership, use and exclusivity of data and AI and machine learning models are clearly defined.

Such measures not only safeguard the commercial viability of their innovations but also allow them to fully capitalize on any downstream developments. Furthermore, the implications of jointly developed IP should be carefully evaluated to ensure both parties share equitably in the benefits and responsibilities that arise from their collaborative efforts.

With AI and machine learning technologies poised to redefine the drug discovery landscape, companies that can strategically manage and protect their IP assets while fostering productive collaborations stand to gain the most.

The delicate dance between collaboration and competition in the era of AI-powered drug discovery demands a new kind of vigilance around IP rights. As such, the role of well-informed, strategically implemented IP management cannot be overstated.

Sequencing the Impact: How AI is Boosting Genomic Medicine

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The rapid development of artificial intelligence (AI) systems will significantly impact businesses that rely on genomic data analysis for research and development of therapeutics and diagnostic decision-making. This article provides an overview of current trends in using AI systems to meet the challenge of extracting clinically useful information from highly complex genomic data.

The Challenge and Promise of Interpreting Complex Genomic Data

While completing the gap-less sequence of the human genome was a milestone for science, the complexity poses a considerable challenge for clinical use of the data, as we have previously discussed. In this post-human genome sequence world, it is becoming increasingly clear that human disease and disease susceptibility are not only a consequence of a particular mutation causing a particular gene dysfunction, but are often a result of genetic variations in non-coding regions, the three-dimensional (3D) structure of the genome, and chemical modifications of the DNA and protein molecules that make up the genome (referred to as the "epigenome").

Taking full advantage of genomic data for therapeutic and diagnostic decision-making will require integrating the linear DNA sequence data of coding and non-coding regions, the 3D genomic structure information, and the epigenome. Information about these different genomic features may come from entirely different data modalities, such as DNA sequencing, imaging, and various biochemical assays. Moreover, accurate therapeutic and diagnostic decisions may require integrating genomic data analysis with medical information and patient data.

Accordingly, AI systems, with their capacity for capturing intricate patterns within large data sets and combinations of different data modalities, could become powerful tools for therapeutic and diagnostic decision-making that can address some of the challenges posed by the human genome complexity.

AI Systems for Interpreting Genomic Data

Recently developed AI systems significantly improve the accuracy of therapeutic and diagnostic predictions. Below, we describe the recent development of AI systems for analyzing information from the non-coding regions in the genome (I), from a combination of different genomic and medical information (II), and from liquid biopsies and 'cell-free DNA (cfDNA) that depend on interpreting genomic data from fragments of the overall genome (III).

I. Interpretation of Non-Coding Genetic Variation in a Three-Dimensional Context

Most genetic variation associated with diseases locate in non-coding regions of the genome. Now that the first gap-less human genome has been completed, the next stage of research and analysis in this field will yield vast non-coding genetic data, which will in turn improve the diagnostic and therapeutic decision-making capabilities of AI systems that can be built on this as-of-yet untapped information.

However, non-coding genetic variants are not as easy to interpret as the coding region genetic variants assigned to a known gene. Variants in coding regions can be interpreted based on knowledge of the particular gene function, which considerably simplifies the analysis. That being said, non-coding variants may regulate different genes depending on the genomic 3D structure and the epigenome. Moreover, non-coding variants may influence the 3D structure and the epigenome. Accordingly, interpreting non-coding variants is a highly complex task that may require more than traditional data analysis.

The rapid developments of AI models show promising results in interpreting genetic data in the 3D context. For example, an AI model (DeepC) can accurately predict topologically associated domains (TADs). TADs are fundamental units of the 3D nuclear organization of the genome that contribute to gene expression by controlling the interaction of gene regulatory regions to their target genes in the 3D space. DeepC predicts TADs using a transfer learning approach and tissue-specific Hi-C data to train models that predict genome folding from megabase (Mb) windows of DNA sequence, which allows prediction of how variations in the primary sequence can impact the 3D genomic structure.

DeepC has been used to address why some people only get mild symptoms from COVID-19, whereas others experience severe respiratory failure and even death. As described in this article, DeepC was able to identify causative single nucleotide non-coding variants and effector genes that may underlie respiratory failure from COVID-19.

These studies demonstrate that AI systems can provide an improved capability to predict disease-linked genetic variants located in the non-coding regions of the genome by taking into account the 3D structure of the genome.

II. Interpretation of Genomic Data in Combination With Different Data Modalities

AI will make analysis of the vast amount of genomic data more accurate and readily available. For example, Moor *et al.* reported on generalist medical AI (GMAI) models that can support clinical decision-making by combining multiple data modalities.

The most active innovation in genomic medicine involves simplifying data analysis for efficient clinical decision-making and combining the various types of genomic data, such as primary nucleic acid sequence data, epigenomic data, structural genomic information, and imaging information of native nucleic acids. The emerging AI models like GMAI will provide efficient and accurate data analysis of a combination of different genomic data modalities and other medically relevant information that will aid accurate diagnostic and therapeutic decision-making.

III. Interpretation of Data From Liquid Biopsy

Liquid biopsy and, in particular, analysis of circulating cfDNA have an enormous potential for clinical treatment and diagnostics. There are currently numerous possibilities for non-invasive screening of disease and monitoring of treatment responses. Recently the analysis of cfDNA also goes beyond detecting variations in the primary DNA sequences to include the methylation levels and structural information such as fragmentation patterns. The complexity of the data currently obtained from cfDNA has rendered traditional data analysis insufficient. AI models have been increasingly used to interpret genomic data from cfDNA to make therapeutic and diagnostic decisions, as explained in this research paper.

Future Opportunities and Challenges of Using AI in Genomic Medicine

AI systems have the potential to revolutionize the development of new treatment and diagnostic options based on human genomic data and spur innovation and growth in the genomic medicine industry. While the new AI systems and their use for interpreting genomic data are exciting, the success of using AI in genomic medicine will require that the AI systems are fully trusted and accepted by the scientific community and society. Moreover, the data analysis from an AI system is only as good as the data provided, so great care must be taken to ensure the quality and accuracy of the data used for the analysis. Access to sufficiently comprehensive quality data may involve data sharing between various businesses, clinics, and government entities. Accordingly, private industry and the government will need to collaborate to ensure the careful use of AI and medical information to successfully develop AI-driven genomic medicine that is trusted and accepted by the scientific community and society.

Safeguarding AI Innovation in Stem Cell Therapy

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The use of artificial intelligence (AI) to advance stem cell therapy has produced exciting results, with a key role in driving recent growth and innovation. Separated into three parts, this article provides an overview of the promises and challenges of stem cell therapy before exploring the current uses of AI to address these challenges. In the third final section, it then outlines strategic considerations for addressing key patent eligibility issues likely to arise when patenting AI-enabled stem cell inventions. Identifying inventions involving a combination of AI and stem cell technology and ensuring appropriate patent protection of these inventions is crucial for safeguarding the advances.

Promises and Challenges of Stem Cell Therapy

The stem cell field has made significant advancements, such as discovering how to induce any cell into a stem cell and how to use stem cells for augmenting muscle regeneration, rebuilding heart tissue, developing brain models (organoids) for studying mental disorders, producing islets for treating diabetes, and many other promising developments as discussed in a recent *Nature Cell Biology* viewpoint article. Moreover, TechSci Research reported that the market for stem cell therapy is expected to grow an impressive 12.39% annually through 2028.

While the stem cell field is rapidly growing, it also faces significant hurdles that need to be overcome. Stem cell therapies require rigorous testing and regulatory approval because stem cells can behave unpredictably during manufacturing and differentiation to functional cell types as discussed in detail in a recent *Cell Stem Cell* article.

That being said, AI is rapidly becoming central for innovative solutions to remove these obstacles facing stem cell therapy.

Using AI to Aid Stem Cell Therapy

Private companies, academic organizations, and government institutions now incorporate AI to find solutions for using stem cells to treat diseases. We discuss below four major areas where AI has already produced promising results.

AI-Enabled Models Predicting Stem Cell Behavior

The Chan Zuckerberg Initiative is building a "virtual cell" to simulate the key features and behavior of any cell type in the human body. The hope is that scientists can use this "virtual cell" to predict how different cells, including stem cells, will respond to external stimuli. This initiative will use the vast knowledge consolidated by global consortiums such as the Whole-Organism Cell Atlas to build a reference map of every cell type in the body. Training AI on such extensive knowledge may provide a system that can accurately predict how cells are generated from stem cells, how they will interact in the human body, how diseases cause loss of cells or cellular functions, and how to use stem cells for curing such diseases.

Dr. Carl Simon and co-workers at the National Institute of Standards and Technology and the National Eye Institute reported a powerful illustration of how AI

can be used to predict cellular behavior and improve stem cell differentiation. This study demonstrated that an AI system can predict the differentiation of stem cells towards eye cells, which was used to significantly improve the quality of this process.

New Tools for Identifying Cells or Cellular States

AI is also providing new tools for identifying cells or cellular states. Dr. Buggenthin and co-workers developed an AI-enabled microscopy imaging system to identify stem cells that initiate differentiation without relying on molecular markers and demonstrated that "lineage choice can be detected up to three generations before conventional molecular markers are observable." Dr. Yang and co-workers demonstrated that such AI and microscopy systems can significantly reduce the variability of stem cell differentiation.

Simultaneously, Dr. Hirose and co-workers developed an AI system called DeepACT that can identify healthy and productive skin stem cells with the same accuracy as humans. This system allows the selection and enrichment of clinically valuable cells.

AI-enabled identification of cells and prediction of their behavior in complex culture systems will help make stem cell differentiation more predictable and improve the production of clinically relevant cells with greater accuracy and efficiency.

Automated Manufacturing of Stem Cells

AI can also provide sophisticated systems for large-scale manufacturing of pure stem cell populations, which is essential for successful stem cell therapy. For example, Nabiha Saklayen (founder of Cellino Biotech) developed a system combining stem cell biology, machine learning, and laser physics to automate stem cell manufacturing. Laser editing allowed both removing unwanted cells and delivering cargo to individual cells. The automated AI-enabled manufacturing of high-quality cell batches may be critical for providing the large numbers of patient-specific cells with low batch-to-batch variability needed for clinical trials and commercialization of stem cell therapy.

Advancing Organ-on-a-Chip Technology

Researchers have previously used stem cells to produce organoids-on-a-chip that offer better clinical predictability of drug properties than conventional cell culture systems, as a study by AstraZeneca demonstrated. Organoids-on-a-chip (sometimes called patients-on-a-chip) are three-dimensional mini-organs that have structural and functional characteristics of native organs. Moreover, Hesperos developed a model system containing several interconnected organs (called human-on-a-chip), allowing an even more sophisticated evaluation of drugs on a system of organs.

While the organoids-on-a-chip technology provides a powerful tool for drug screening and validation, this technology is difficult to scale because of variability from organoid to organoid, and it is labor-intensive to make them work on a large scale due to the complexity of these systems. Dr. Bai and co-workers reviewed multiple ways of addressing this issue using AI systems. In particular, AI can aid with bioprinting of organoids to facilitate the automation of manufacturing organoids-on-a-chip with reduced variability, as reported by Dr. Lee.

Accordingly, combining organ-on-a-chip technology with AI will significantly boost stem cell-based drug discovery and validation by providing improved methods for producing high-quality organoids.

Strategies for Patent Protection of AI-Enabled Stem Cell Technology and Satisfying the Patent Eligibility Requirement Under 35 U.S.C. § 101

The increased use of AI in stem cell research and clinical development of stem cell therapies will generate many opportunities for innovation and growth, as shown above. Intellectual property rights will be particularly important for driving innovation in this area, as advances will require the collaboration of various companies, academic organizations, and government institutions, which all have different expertise and available resources. Collaboration among all these different actors often results in intellectual property concerns, in particular, patent owner rights to inventions existing before the collaboration as well as inventions arising from the collaboration.

Stakeholders should carefully monitor inventions from combining AI and stem cells and look for patent-eligible concepts at every stage to avoid issues that would frustrate commercial interests. In this regard, it is important to consider 35 U.S.C. § 101 of the Patent Act because it determines what categories of inventions are patent-eligible if the other requirements are met and can be a crucial hurdle to overcome for many types of inventions.

Patent Eligibility Requirement Under 35 U.S.C. § 101

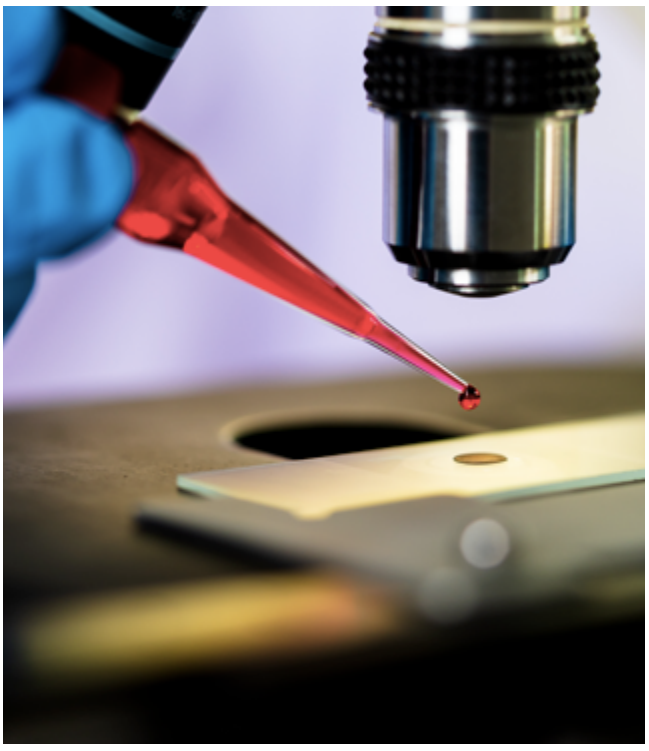
Section 101 of the Patent Act states that processes, machines, manufactures, and compositions of matter, as well as improvements thereof, are eligible for patent protection. Interpreting this statute, the U.S. Supreme Court ruled in *Diamond v. Chakrabarty*, 447 U.S. 303 (1980) that man-made living organisms are eligible for patent protection, but also affirmed that no patents should be granted on laws of nature, natural phenomena, and abstract ideas. Later, the Supreme Court decisions in *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 573 U.S. 208 (2014) and *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66 (2012) set forth a two-part test for determining patent eligibility that can pose a significant obstacle to patenting certain software and computer-implemented systems like AI. The Mayo/Alice test first determines if the claims are directed to a judicial exception, such as an abstract idea, a law of nature, or a natural phenomenon. If the claims are directed to a judicial exception, then the second step determines whether the claim recites additional elements that amount to significantly more than the judicial exception.

While living organisms and biological molecules may be patent-eligible if they are man-made, the Supreme Court in *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576 (2013) determined that isolated DNA is a naturally occurring product and patent-ineligible subject matter under 35 U.S.C. § 101. Moreover, *In re Roslin Institute (Edinburgh)*, 750 F.3d 1333 (Fed. Cir. 2014) it was concluded that the claims were directed to a cloned farm animal, such as a sheep, and therefore not "markedly different" from a naturally occurring animal. Patent eligibility of living organisms and biological molecules will therefore require showing that the invention is markedly different from its naturally occurring counterpart.

Strategies for Overcoming the Patent Eligibility Requirement Under 35 U.S.C. § 101

While satisfying the patent eligibility requirement is determined on a case-by-case basis and will be very fact-dependent, the court decisions addressing these issues provide some general strategies for overcoming patent eligibility issues. Below are three approaches that may be particularly relevant when seeking to protect AI-enabled stem cell technology.

a) Does the claimed invention improve or solve a problem facing stem cell therapy?



Even if the Mayo/Alice test has created difficulties in obtaining software patents on some computer-implemented technology, an invention deemed directed to patent-ineligible subject matter has nevertheless been found patent-eligible if the claimed invention provides technological improvement. *See, e.g., Enfish, L.L.C. v. Microsoft Corp.*, 822 F.3d 1327, 1336-37, (Fed. Cir. 2016) where the patentee successfully argued that its claimed self-referential table for a computer database was an improvement to an existing technology and thus not directed to an abstract idea. In *CardioNet, L.L.C. v. InfoBionic, Inc.*, 955 F.3d 1358 (Fed. Cir. 2020), the U.S. Court of Appeals for the Federal Circuit found the claimed cardiac monitoring system patent-eligible because it was not merely an abstract idea of distinguishing between atrial fibrillation and flutter caused by irregular heartbeats, but achieved improvement over conventional monitoring devices. Demonstrating technological improvement was also successfully used to satisfy the patent eligibility requirement in, for example, *Visual Memory LLC v. NVIDIA Corp.*, 867 F.3d 1253 (Fed. Cir. 2017), *Amdocs (Israel) Ltd. v. Openet Telecom, Inc.,* 841 F.3d 1288 (Fed. Cir. 2016), and *Rapid Litig. Mgmt. v. CellzDirect, Inc.*, 827 F.3d 1042 (Fed. Cir. 2016).

Therefore, AI systems that significantly improve stem cell technology could overcome patent eligibility issues by arguing for technological improvement over conventional methods or devices. Practitioners drafting applications to cover AI inventions in the stem cell field that may raise a patent eligibility issue should describe how the claimed inventions improved or solved a problem facing stem cell therapy to provide evidence of technological improvement.

b) Do the claims covering a stem cell recite features markedly different from naturally occurring counterpart cells, and can AI help identify such features?

The patent eligibility requirement under 35 U.S.C. § 101 also causes problems for claims directed to stem cells if the claimed cells are not shown to be different from the in vivo counterpart cells. *See Ass'n for Molecular Pathology v. Myriad Genetics, Inc.* and *In re Roslin Institute (Edinburgh).*

Patenting stem cells therefore relies on whether it can be shown that the claimed cells are markedly different from naturally occurring counterparts. For example, in *Ex Parte Ho*, Appeal No. 2016-007472 (PTAB, 2018), the patentee successfully argued that the specific stem cell culture conditions resulted in structural differences between in vivo and in vitro mesenchymal stem cells (MSCs), and the claims recited MSCs with higher expression levels of specific markers compared to the naturally occurring counterpart cells. While *Ex Parte Ho* is an appeal decision by the Patent Trial and Appeal Board and therefore not binding case law, this decision highlights the importance of identifying features or behaviors of stem cells in culture that could distinguish them from their naturally occurring counterparts.

The rapid advances in using AI to identify and characterize stem cells may result in the discovery of features of stem cells in culture that are not present in vivo, and may provide new options for satisfying the patent eligibility requirement for stem cells.

c) Identifying combinations of steps that result in non-conventional methods even though the individual steps are well-known.

The Federal Circuit decision *Rapid Litig. Mgmt. v. CellzDirect, Inc.*, 827 F.3d 1042 (Fed. Cir. 2016) found a claimed combination of freezing and thawing steps patent-eligible. While the individual steps of the claims were well-known, the court found that the combination of steps was "far from routine and conventional" and provided technological improvement of cell viability.

In view of the *CellzDirect, Inc.* decision, it is important to consider that integrating AI systems and stem cell technology may result in patent-eligible processes even though the individual steps of the newly developed methods are well-known.

Conclusion

AI has already produced promising results for the development of stem cell technology, as discussed above. Still, the full-scale deployment of these therapies will require further technological development, which can be boosted by the availability of high-quality data for training AI systems and the use of these AI-enabled technologies to produce biological insights into the properties and behavior of stem cells. Further, identification of patent-eligible subject matter arising from the convergence of AI and stem cell technology is vital for safeguarding progress and facilitating collaboration among the various actors involved.

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