Atlas Regeneration, Inc.

Atlas Regeneration is dedicated to the development of novel data-driven solutions for regenerative medicine, adapting proven technologies, and analysis strategies to take a multiomics-wide view of stem cell quality and cell fate design. Our core offering is a global comprehensive map of stem cell differentiation, Universal Signalome Atlas for Regenerative Medicine, reflecting the pathway activation states across all characterized stem cells and their differentiated products. Key applications of Universal Signalome Atlas for Regenerative Medicine will include quality assurance for engineered cell products, and directed regeneration pharmacology, where we will screen and identify compounds that can efficiently convert pluripotent cells into desired subtypes. Another marketable piece of IP is development of specialized signaling pathway analysis systems Regeneration Intelligence which supposed to target the unmet needs of determination and prediction of stem cell signaling pathway activation to govern cell differentiation in specific directions.

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We take a full advantage of clinical, health, gene–gene, and gene–environment interactions information, obtained from Big Data, in other words, large datasets from different types of bioinformatics, chemical and genomic data, using deep learning (DL) and advanced artificial intelligence approaches. Specifically, our in-house pipeline applications include systems that can analyze large collections of data to identify genes and targets that may be responsible for certain types of cancer, predict alternated pathways corresponding to certain conditions, predict polypharmacology profile of molecules and perspective drug candidates, and recognize objects in medical images or scans. Using our drug discovery platform, we also identify and rank drug–disease, drug–target and target–disease associations.

Aging is an issue that effects all people around the globe universally, but as the baby boomer generation ages, the stress that it

places on society becomes greater and the need to develop methods for people to remain productive as they age rises in turn. Aging is a very complex multifactorial process that cannot be stopped or reversed by a simple combination of drugs, which is why it is important to develop personalized treatments tailored to individual subjects. The pharmaceutical industry needs a platform to effectively utilize and clinically implement stem cell technologies.

Another aspect of the company's specialization is screening and predicting the effectiveness of possible regeneration-inducing drugs in a high-throughput environment to at least slow some of the aging processes by stimulating the potential of natural tissue regeneration. Some of the known drugs have been in the market for many decades and only recently scientists have started finding clues to their anti-inflammation, regeneration, and protective effects. There is an urgent need

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for intelligent systems that will cost effectively predict the effectiveness of many drugs on individual tissue, organ, and organism levels.

Company history

The project ‘Atlas Regeneration’ began in 2014, after the annual conference in regenerative medicine organized by the Wake Forest Institute for Regenerative Medicine, where a team of leading bioinformaticians met with Dr Anthony Atala and embarked on the idea of creating a comprehensive map of all cellular differentiation states along with mechanisms to intelligently direct vertical and horizontal differentiation. As a scientist and practicing physician, Dr Atala had been formulating strategies where bioinformatics could be used to overcome existing challenges. The company was formed to address the critical needs of regenerative medicine and to discover new drugs to extend healthy longevity. Atlas Regeneration Inc., as a company dedicated to developing novel software platforms and algorithms for drug discovery relating to regenerative medicine and stem cell research, was established in 2015 [1].

Atlas created a *de novo* proprietary database of almost three hundred linearized maps of cell signaling pathways related to regeneration. Each pathway was manually curated to meet highest quality standards (to contain constantly updated information based on current literature) and to fit to innovative logic of Atlas signal transduction scoring algorithm. Simultaneously Atlas developed its unique pathway analysis scoring platform Regeneration Intelligence which allows it to utilize transcriptomic, proteomic, and epigenetic data to calculate the potential of signaling pathway activation or actual pathway activation scores. Based on these results, Atlas team demonstrated the close resemblance of iPSCs with ESCs at the pathway level, and provided examples of how pathway activity analysis can be applied to identify iPSC line abnormalities or to predict *in vitro* differentiation potential. The results indicate that pathway activation profiling is a promising strategy for evaluating the safety and potency of iPSC lines in translational medicine applications allowing scientists to test differentiation abilities of many iPSC lines *in silico* while saving valuable time for patients waiting for treatment. This work leads to first company publication in the journal *Oncotarget*: “Quantifying signaling pathway activation to monitor the quality of induced pluripotent stem cells” [2,3]. In 2015 Atlas partnered with InSilico Medicine, to build a state of the art platform Universal Signalome Atlas for Regenerative Medicine to select and to rate personalized proregeneration therapies and to identify new drug candidates in regenerative medicine.

Based on chemical libraries of high-throughput *in vitro* experiments (over 50 M experimental data

points), we developed deep learning models for most known druggable targets. DL is especially suitable for modeling big data on this scale or larger. Along with screening molecules through DL predictive models, we also perform docking to evaluate the same targets from a different perspective.

While at the seed stage, Atlas offers commercial services to other companies for the safety evaluation of cells, as well as their differentiation potential. One of the promising directions is personalized regenerative medicine, where pharmacology intervention is based on patient genetic and epigenetic profiles of the patient.

What the company does?

Regeneration bioinformatics

Using big data analysis tools, Atlas Regeneration develops cellular state navigation systems, where differentiation and reprogramming methods could be predicted and simulated *in silico*.

Personalized regenerative medicine

Personal individuality is important, so the most successful interventions should be based on the patient’s own genetic background. As more relevant information becomes available, we are developing diagnostic and prognostic protocols for personalized regenerative medicine.

Geroprotector screening & validation

We use advanced multi-omics tools to find new drugs or repurpose already existing drugs that can slow down aging and combat disease.

Quality control & standards

Atlas conducts extensive research that helps to identify and set the standards for the various cell and tissue types setting the norms for gene expression, metabolomic and epigenetic profiles.

Regeneration pharmacology

We utilize *in silico* approaches to screening for drugs and nonpharmacologic interventions that may be used for *in vivo* reprogramming and activation of endogenous repair mechanisms.

Preventative regeneration

Some tissues degrade faster than the others leading to loss of function and failure. Our technology may be applied to recognize sources of potential problems early and devise preventative strategies for early interventions.

New targets identification

Computational target identification and mechanism-of-action inference for known diseases.

Drug synergy prediction

A quantitative assessment of drug–drug interactions, side effects and toxicity.

Current results & commercialization**Drug discovery**

Using pathway-based target identification and *in silico* drug discovery, Atlas is able to discover drugs or drug combinations to: modulate cellular states, direct differentiation, prevent and control tumorigenicity, and induce and modulate systemic and tissue-specific endogenous regeneration potential. The core of the technology is the ability to integrate and analyze extremely diverse datasets of structured and unstructured data. For example, we can combine clinical data with gene expression, signaling pathways and chemical features of molecules. Our platform leverages mutation, copy number variation, proteomics, metabolomics, and *in vivo* data with bioinformatics and cheminformatics analysis. Commercialization track: license the *in silico*/preclinical data to pharmaceutical companies along with drug discovery services and/or contracting research.

Standards in the stem cell field

We developed bioinformatics algorithms which allow us to evaluate cell differentiation propensity using corresponding transcriptomic data that dramatically reduce cost of analysis and evaluation time. Using the Atlas proprietary pathway analysis system, we demonstrated that pathway activation profiling is a promising strategy for evaluating the safety and potency of cell lines in translational medicine applications, allowing scientists to test differentiation abilities of many lines *in silico* while saving valuable time for patients waiting for treatment. Our algorithm allows for the correct identification of signaling pathways previously confirmed *in vitro* experiments. The innovative Atlas approach uses unique maps of signaling pathways and special algorithms (patent pending) which allow the establishment of strong statistical inference between the models and actual *in vitro* experiments. Commercialization track: sell licenses to test the signaling pathway activation profiles of cell and tissue profiles against databases, and to establish safety ratings.

References

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- 2 Makarev E, Fortney K, Litovchenko M, Braunewell KH, Zhavoronkov A, Atala A. Quantifying signaling pathway

Future strategy**Personalized regenerative medicine**

Personalize drug combinations for individual patients and for individual cases (e.g., oil burns vs dry burns). Personalize therapies to the patient- and tissue-specific microenvironment. Develop personalized cell–drug and other drug combinations

Contract research

Atlas regeneration tests the pathway activation profiles in cells/tissues provided by contractors. *In silico* prediction of the effects of the various drugs (or any other actionable biological molecules) on specific cells/tissues.

Core values**Vision statement**

When cutting edge biomedical research meets state-of-the-art big data technologies, the extraordinary seems possible. At the forefront of scientific innovation is the recognition that limited regeneration abilities are not inevitable facts of life; instead they are biological challenges with real solutions.

Mission statement

To benefit our society by using big data, artificial intelligence and bioinformatics resources to help accelerate health and longevity advances in all areas of regenerative science and medicine.

Goals

To be the world's leading big data artificial intelligence driven discovery and service resource entity for the biomedical field. The goal of Atlas Regeneration is to develop and make available to the biomedical community novel data driven technologies and services that address the unmet needs of the regenerative medicine market.

Financial & competing interests disclosure

E Makarev is an employee of Atlas Regeneration Inc. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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