Rizzoli Orthopaedic Institute looks for genetic insights in the family tree

Overview

The Need
Italy's Rizzoli Orthopaedic Institute sought stronger tools to study the genetic underpinnings of rare hereditary bone diseases.

The Solution
Rizzoli engaged IBM Research to develop a first-of-a-kind pedigree analytics platform that integrates genomic data, medical images and family history into a powerful research tool.

What Makes it Smarter
Using algorithms developed by IBM Research, Rizzoli's solution identifies "cluster" patterns within family trees to guide researchers in the development of more effective treatments.

The Result
"With IBM's experience and technology, we're positioning ourselves to gain new insights into how we can treat hereditary diseases."

— Luca Sangiorgi, manager, Medical Genetics Unit, Rizzoli Orthopaedic Institute

When researchers completed the first-ever map of the human genome earlier this decade, it marked the beginning of a new era of molecular and biological research, one that promised a much deeper and more detailed understanding of how the human body works. The direct result of the effort—a map of the identity, location and function of the more than 20,000 genes that make up the human genome—is as profound as it is fundamental, since it lays the foundation for a whole new range of scientific discoveries. The breakthrough's most important expected benefit is that it will provide scientists with the basis to unravel—and ultimately pinpoint—the relationship between specific genes and complex medical disorders.

The main implication of improved genomic understanding is the revolutionary impact it is expected to have on the diagnosis and treatment of disease. One aspect of this vision is the use of genetic testing to screen patients for specific gene mutations that indicate a higher risk for specific diseases, and thus provide a cue for increased vigilance. Another is the ability to develop "targeted" treatment protocol for each patient based on the genetic signature of the disease. For researchers and clinicians, the biggest challenge to realizing this vision is the extreme complexity of the underlying dynamics of how specific genetic mutations lead to specific diseases. That's because some disorders can result not only from a single genetic mutation, but from different types of mutations, from the interplay of multiple genes, from a mix of genetic and environmental factors—or from some combination of the three.

The complex roots of hereditary disorders

In addition to having complex genetic roots, diseases can also vary in their phenotype—the way they manifest their symptoms or outward characteristics within specific patients. To researchers, the correlation

Business Benefits

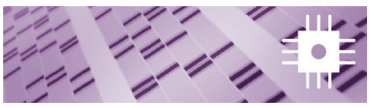
- More effective treatments for hereditary diseases through more targeted protocols
- More accurate determination of hereditary disease risks
- More informed basis for disease screening, enabling fewer unnecessary tests, thus reducing costs
- Reduction in physician errors

between genotype and phenotype represents an important window into the complex genetic interactions that lead to disease. In the study of hereditary diseases (those caused by mutated genes inherited from one or more parent), even deeper insights can potentially be achieved by analyzing the intersection of genotype and phenotype data throughout each patient's family tree. To test this premise, the Rizzoli Orthopaedic Institute—a research hospital whose Medical Genetics Unit specializes in rare hereditary skeletal diseases—selected IBM to develop a first-of-a-kind analytics system to uncover new insights into the genetic causes of hereditary diseases. Known as the Pedigree Visualization and Analytics Platform, Rizzoli's solution combines the three essential viewpoints of hereditary disease research—genotype, phenotype and family history—into a powerful and integrated analytical tool. In the analysis of hereditary diseases, family pedigree is ground zero. That's why the solution—being developed by the IBM Haifa Research Lab—provides researchers with the means to analyze such diseases within the framework of family medical history.

Insights from the family tree

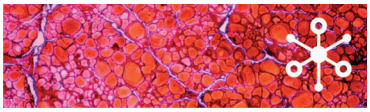
While tracking hereditary diseases across the family tree can tell researchers a lot, granularity is the key to unlocking insights. For each member—or node—in the family tree, genomic data can tell researchers whether that person carries a particular mutation, or a variation thereof. Because the solution enables them to "drill down" into each node, researchers can see not only whether the member is carrying a mutation (genomic profile), but also whether and how that mutation is expressed physically (phenotypic profile) in the form of medical images, such as x-rays. By performing this kind of analysis across all nodes of a patient's family tree, researchers are able to detect patterns that they can test and further investigate. One potential outgrowth of this analysis is a more precise, evidence-based assessment of each family member's underlying risk of acquiring the disease.

Smarter Healthcare: Deeper insights through "pedigree" analytics



Instrumented

The Rizzoli solution extracts and integrates clinical, genomic and medical imaging data into a rich, granular dataset.



Interconnected

Open interfaces enable the Rizzoli solution to share data with other institutions and add new services, content sources and research partners.

Intelligent

Advanced algorithms identify correlation patterns within genotype and phenotype data to guide deeper investigation by researchers.

Solution Components

Software
- IBM Enterprise Content Manager
- IBM WebSphere® Application Server
- IBM InfoSphere™ Warehouse
- IBM Tivoli® Directory Server
- IBM Tivoli Storage Manager

Servers
- IBM System x® 3400

Services
- IBM Haifa Research Lab
- IBM First-of-a-Kind Program

"Understanding the complex roots of hereditary diseases requires a whole new way of looking at pedigree analytics."

—Luca Sangiorgi

Given the large number of variables and the complexity of the data, the task of identifying the most meaningful underlying patterns poses an inherent challenge to researchers. Rizzoli and IBM realized that while trial and error are a natural part of the analysis, applying intelligence would significantly enhance researchers' ability to find the patterns in the data. To enable this, IBM Research is developing a tool that enables pedigree clustering from a variety of angles, thus helping researchers to discover and better understand correlations between genotypic and phenotypic data. In addition to streamlining the research process, the insights derived from this complementary capability provide guidance to Rizzoli physicians in offering the most effective treatment options.

The defining quality of the solution's architecture is the use of open interfaces such as HL7 and DICOM to integrate all the necessary sources of information throughout the hospital. IBM Enterprise Content Manager, running on IBM WebSphere® Application Server, is the core of the solution, responsible for accessing, storing and managing all information assets used in the pedigree analysis. This includes medical imaging data retrieved from sources such as the hospital's PACS systems as well as clinical and genomic information from hospitals, labs and clinics. User authentication is performed by IBM Tivoli® Directory Server, while IBM Tivoli Storage Manager handles the long-term archiving and life-cycle management of the imaging assets. Running on IBM System x® servers, the solution is being developed within IBM's First-of-a-Kind (FOAK) program, under which IBM researchers and their inventions are brought together with clients and partners in the marketplace to solve business problems and seize new growth opportunities.

Flexibility for a dynamic environment

Rizzoli implicitly recognized the need for a solution that could adapt to the changing healthcare landscape. Among the most important requirements was the need to enable the exchange of clinical, imaging and genomic data with other healthcare institutions. This reflects the fundamental idea that when it comes to healthcare analytics, more data tends to lead to better insights—benefiting all institutions engaged in it. In the case of Rizzoli, the need to gather medical information from multiple family members, spread across multiple hospital record systems, was the most direct driver. To ensure this, Rizzoli specified compliance with key health data standards like HL7 (for family history), DICOM (for medical images) and appropriate IHE profiles such as PIX/PDQ (for cross-hospital patient ID correlation). Even more important to Rizzoli, however, was the need for a partner who had both a strong knowledge of these standards, healthcare domain best architecture practices and a deep track record in implementing them across healthcare institutions. It saw IBM as having all of these qualities.

The other major dynamic influencing the solution's design is the growing diversity of tools, partners and other information sources expected to become an increasingly important part of the healthcare informatics ecosystem. Rizzoli recognized the importance of designing a solution that could easily be extended to include such new components as they became available. Equally important was the flexibility to reuse existing components within its enterprise to develop new analytical capabilities. IBM's answer was to design an SOA-based medical imaging repository that integrates all key components over an enterprise service bus—into which new analytical services, content sources or other partners can be easily and cost-effectively connected.

The most important potential benefit of Rizzoli's new approach to pedigree analytics is a general improvement in the treatment of hereditary diseases, made possible by a quantum leap in understanding the complexity of the genetic interactions underlying them. This has the potential to enable Rizzoli to offer more targeted and effective treatment protocols for sick patients, while more accurately assessing the underlying risk for each family member based on a rigorous analysis of genotypic and phenotypic data. To Luca Sangiorgi, manager of Rizzoli's Medical Genetic Unit, the solution exemplifies the new tools researchers are applying to solve an old puzzle. "Understanding the complex roots of hereditary diseases requires a whole new way of looking at pedigree analytics," says Sangiorgi. "With IBM's experience and technology, we're positioning ourselves to gain new insights into how we can treat hereditary diseases."

For more information

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