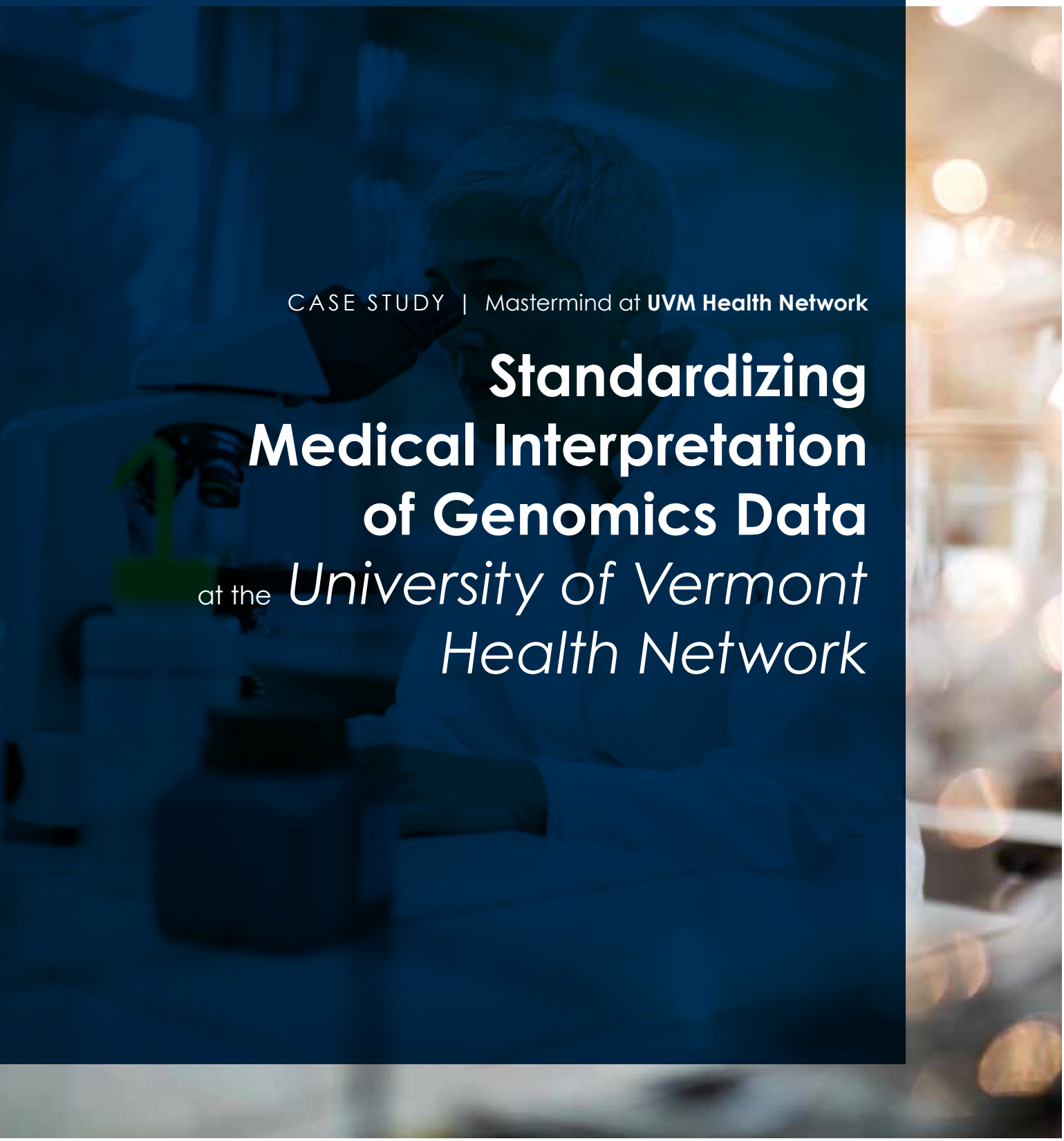
GENOMENON®
POWERING EVIDENCE-BASED GENOMICS



CASE STUDY | Mastermind at **UVM Health Network**

Standardizing Medical Interpretation of Genomics Data

at the *University of Vermont Health Network*

CASE STUDY

Mastermind at **UVM Health Network**

"Genomenon offers a clinical solution to effectively standardize the way we are searching the medical literature in our clinical practice. We can now lock down this process, which includes pathologists sending reports with a clinical finding substantiated by the medical literature."

Dr. Nikoletta Sidiropoulos, Medical Director of Genomic Medicine,
Department of Pathology and Laboratory Medicine,
University of Vermont Health Network

EXECUTIVE SUMMARY

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UVM HEALTH NETWORK'S VISION

- Improve health care through genomic medicine for the 1M+ patients in the UVM network.
- Deliver genomic medicine through CLIA-licensed & CAP-accredited internal laboratories.
- Integrate patient care, education, and research in a caring environment.

CHALLENGES

- Lack of thoroughness of genomic literature search tools for variant curation.
- Standardizing the variant curation process across the UVM's clincal team to handle an increasing caseload.

APPROACH

- Integrate the best genomic analysis technologies, people, and processes within the lab.
- Standardize on Mastermind to ensure a consistent literature search process.
- Leverage Mastermind to comprehensively vet the medical literature for each patient case.

ACCOMPLISHMENTS

- Built standardized operating processes for variant curation.
- Significantly reduced variant curation times.
- Assurance that each case is comprehensively vetted with confidence in their due diligence assessing and reporting on a patient's case.

CASE STUDY

Mastermind at **UVM Health Network**

MASTERMIND®

COMPREHENSIVE GENOMIC SEARCH ENGINE

"Using Mastermind and not just putting in random association words in Google Scholar or PubMed has been tremendously useful in generating appropriate medical literature in support of our reports in clinical practice."

Dr. David Seward, MD PhD,
Assistant Professor of Pathology and Laboratory Medicine, College of Medicine, University of Vermont

THE UVM HEALTH NETWORK

The University of Vermont (UVM) Health Network, an integrated health care system with six hospitals, serves over one million residents of Vermont and northern New York. The community of more than 4,000 regional healthcare professionals provides collaborative, cost-effective, quality care while sharing knowledge and resources to deliver optimal patient care across all sites.

In 2013, the leadership team decided to forego classical molecular pathology – which predominantly targets single genes with limited scope – and to incorporate Next-Generation Sequencing (NGS) technology into their CLIA (Clinical Laboratory Improvement Amendments)-licensed and CAP (College of American Pathologists)-accredited laboratories.

BUILDING A STANDARDIZED AND SCALABLE VARIANT INTERPRETATION PROCEDURE USING MASTERMIND

"The exercise of searching the medical literature to annotate the medical relevance of variants is not a process that had been locked down," Dr. Nikoletta Sidiropoulos (Medical Director of Genomic Medicine, Department of Pathology and Laboratory Medicine) says. "Genomenon offers a solution to standardize the way we are now searching the medical literature in our clinical practice. We can lock down the process for pathologists sending reports with a clinical finding that has been substantiated by the medical literature."

Mastermind's intuitive interface allows clinicians and pathologists to quickly identify clinically relevant medical literature on variant-disease relationships. Starting with simple questions such as "has a variant been found in the research, and if so, does it have a functional impact?", one can quickly determine whether a variant has been sequenced in a particular tumor. The new standardized procedures with Mastermind ensure that any clinician can efficiently communicate identified results, with supporting evidence, to expedite clinical care or clinical trial enrollment.

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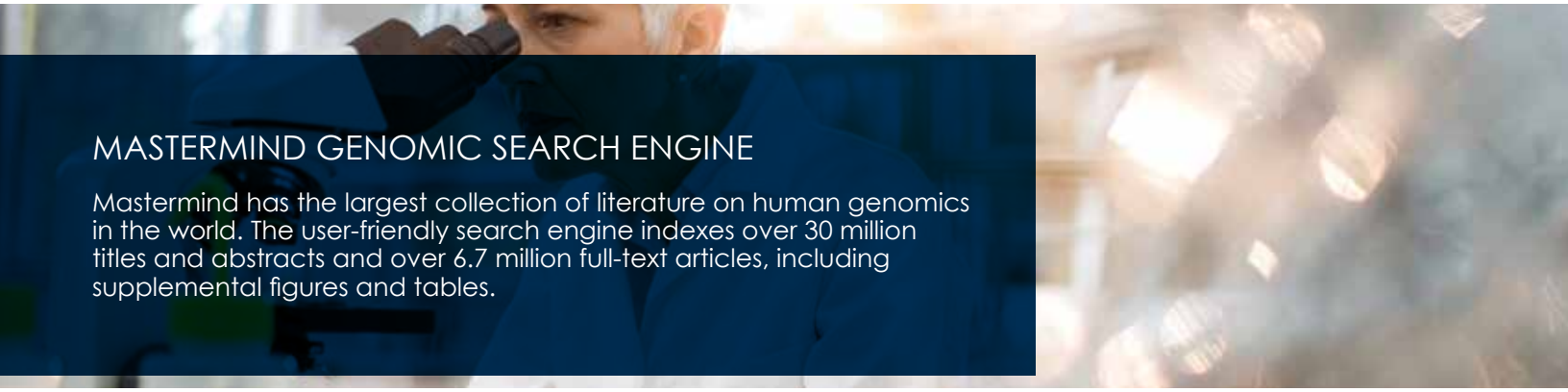

MASTERMIND GENOMIC SEARCH ENGINE

Mastermind has the largest collection of literature on human genomics in the world. The user-friendly search engine indexes over 30 million titles and abstracts and over 6.7 million full-text articles, including supplemental figures and tables.

MASTERMIND PROVIDES SUPPORTING EVIDENCE OF NON-SMALL CELL LUNG CANCER THAT LEADS TO ENROLLMENT IN A POTENTIAL CLINICAL TRIAL

The highest volume of cases currently sequenced at UVM Health Network are non-small cell lung cancer (NSCLC). Most critical with these cases is an exact diagnosis resulting in proper treatment or the patient joining an available clinical trial. This requires a thorough analysis of the functional role of the identified mutation(s) and their roles in tumor progression. Mastermind – with its rich medical variant-to-disease knowledge base – has become integral for uncovering the underlying genetic role of these lung cancer cases.

The example of a clinical case with a known somatic KRAS variant (p.G12C) and an additional CDKN2A variant (p.H83Y in p16/INK4A) highlights the incorporation of Mastermind into the clinical interpretation process for reporting at UVM Health Network. Mastermind uncovered that the CDKN2A variant leads to a loss of function of this tumor suppressor gene. Specifically, this mutation leads to the inability of p16 or CDKN2A to stop the cell cycle, or cell-cycle arrest (Author et al., Oncotarget, 2014). When the evidence from the medical literature is strong and supporting, the information is immediately incorporated into the clinical pathology report for the oncologist at the UVM Health Network.

"The advantages of Mastermind lie in the advanced search capabilities, which allow me to search only for only publications that studied combined KRAS and CDKN2A mutations – a huge time saver" Dr. David Seward (Assistant Professor of Pathology and Laboratory Medicine) says. This instance identified that these combinations of mutations are associated with tumors that would be sensitive to checkpoint inhibitors (Dietlein et al., Cell, 2015) and a common therapy would include Chk1 and MK2 inhibitors. These findings were incorporated into the final clinical report and prompted a recommendation to enroll this particular patient in a specific clinical trial.

MASTERMIND FEATURES

- Actionable data on over 4.9 million genomic variants
- Search results are prioritized by clinical significance
- Designed and optimized for pathologists, geneticists, and variant scientists
- Significantly faster and more comprehensive than PubMed or Google Scholar searches
- Updated weekly with the latest articles

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