Alissa Interpret
The next evolution of Cartagenia

Alissa Interpret, part of the Agilent Clinical Informatics platform, supports clinical genetics and molecular pathology labs to automate their variant assessment and reporting workflows. With Alissa, they perform triage, assessment, curation and reporting for routine diagnostic testing, build the lab's internal knowledge base; access a wealth of annotation sources and peer reviewed databases, and draft lab reports with ease.

These Case Studies show how our customers, with the help of our team of Field Application Scientists, have established their lab's routine diagnostic pipelines on Alissa. You'll learn how labs use Alissa to improve their turnaround times, implement their NGS workflows for arrays, panels and exomes, and address clinical interpretation challenges, from clinical genetics to molecular pathology.

**Alissa Interpret Case Study Summaries**
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**Clinical Genetics**
#1 Comprehensive Genomic Analysis of Complementary Microarray and Next Generation Sequencing Data for Clinical Diagnostics

#2 An Efficient Clinical Pipeline for Microcephaly, RASopathy and Leukodystrophy Gene Panels Using Alissa Interpret's Flexible Classification Functionality: The Hopitâl Robert-Debré Experience

#3 Implementing ACMG Guidelines on Sequence Variant Interpretation: Software-Assisted Variant Curation and Filtering

#4 Whole-Exome Sequencing Diagnostics for Patients with Intellectual Disability at UMC Utrecht: A Tiered and Automated Approach Using Alissa Interpret

**Molecular Pathology**
#5 Identifying Somatic Tumor-Only Variants with Intelligent Variant Filtration Strategies in Alissa Interpret

#6 Challenges in Molecular Pathology: NGS variant Assessment and Reporting on Actionable Findings
#1 Comprehensive Genomic Analysis of Complementary Microarray and Next Generation Sequencing Data for Clinical Diagnostics

Recently, next generation sequencing (NGS) has proven its diagnostic utility for a growing range of clinical applications. The intent being to replace a multitude of primary molecular diagnostic tools, such as Sanger Sequencing, qPCR, MLPA and array-based copy number analysis (aCNA), with a single methodology. However, extraction of copy number variations (CNVs) from NGS data has been challenging. In this case study, Greenwood Genetic Center illustrates the successful application of both NGS and aCNA as complementary methods for clinical diagnostics. This illustration is an example of how the Alissa Interpret software module serves as an integrated data analysis platform allowing joint analysis of CGH and NGS assay results. This Case Study will show you:

- How Greenwood Genetic Center brings together NGS and Array results in routine genetic testing for improved diagnostic yield.
- How Alissa Interpret allows for a seamless integration of copy number and molecular variants.
- An illustration on how Greenwood Genetic Center used this feature to address a diagnostic case of Brittle Cornea.

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#2 An Efficient Clinical Pipeline for Microcephaly, RASopathy and Leukodystrophy Gene Panels Using Alissa Interpret’s Flexible Classification Functionality: The Hôpital Robert-Debré Experience

Combining gene panels with next generation sequencing (NGS) has provided a fast and cost-efficient way to assay mutations and relate them to specific pathologies. For a given panel, NGS makes it possible to test all sequences in parallel without substantially increasing the cost. This is leading to a new clinical practice in which all known contributing genes of a pathology can be assessed at first evaluation. However, the results of such an analysis may be quite complex, involving up to thousands of variant calls that should be sorted and filtered with great care to arrive at results with clinical significance. In this case study, we illustrate how a French pediatric hospital, Robert-Debré, has implemented Alissa Interpret, the variant assessment module in the Agilent Alissa Clinical Informatics platform, to automate and manage variant assessment in their NGS workflow. This Case Study will show you:

- How the molecular geneticists at the Robert-Debré hospital save time by using Alissa Interpret to set up a variant classification strategy that helps diagnose patients suffering from rare developmental pathologies.
- How Alissa Interpret can be used in a flexible way, through the extensive labeling and variant review functionality.
- How Robert-Debré strengthens its clinical pipeline by using its patient population statistics
- How the molecular lab at Robert-Debré has built a valuable knowledge base using the Alissa Interpret Managed Variant List (MVL) capabilities.

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#3 Implementing ACMG Guidelines on Sequence Variant Interpretation: Software-Assisted Variant Curation and Filtering

Since their publication in 2015, the standards and guidelines of the American College of Medical Genetics and Genomics (ACMG) have been widely adopted. The College made these available as an educational resource for clinical laboratory geneticists to help them in the interpretation of sequence variants. Although adherence to these standards and guidelines is voluntary and cannot replace the clinical laboratory geneticist’s professional judgment, the recommendations represent a broad consensus of the clinical genetics community. With increasing volumes and the use of large gene panels (clinical, full exomes and even full genomes) in clinical genetics routine practice, labs need strong informatics tools that support them in benefit from community standards, and to keep up with the best standard of care. This case study will show you:

- How Uppsala University Hospital’s Molecular Genetics lab has implemented the ACMG guidelines and standards on sequence variant interpretation.
- How Alissa Interpret facilitates automation of variant classification pipelines.
- How the ACMG classification functionality enables evaluation of all ACMG criteria on a single variant level providing a complete evidence overview.

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#4 Whole-Exome Sequencing Diagnostics for Patients with Intellectual Disability at UMC Utrecht: A Tiered and Automated Approach Using Alissa Interpret

Diagnostic trio Whole-Exome Sequencing (WES) has proven to be an important tool for diagnosing heterogeneous genetic diseases. Especially for patients with syndromic or non-syndromic intellectual disability, WES is increasingly being used as part of the genetic diagnostic workup. To provide the best standard of service to its referring physicians and their patients, the Genome Diagnostics laboratory at the University Medical Center Utrecht (UMC Utrecht) has set-up its ISO15189:2012 accredited exome analysis and reporting pipeline in accordance with the recommendations of the European Society of Human Genetics and the Health Council of the Netherlands. Key aspects of these recommendations that have been implemented include: Informed consent procedure with focus on patient autonomy, protocolled procedure for reporting of unsolicited findings, and international collaboration and data sharing to facilitate the interpretation of genomic data. This case study will show you:

- How the UMC Utrecht has implemented an automated and tiered approach for WES diagnostics using Alissa Interpret.
- How UMC Utrecht’s tiered analysis workflow has been used for a specific clinical case.
- How the tiered approach maximizes clinical utility and time efficiency, while minimizing uncertain and unsolicited findings.

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How pathology labs adopting NGS technology can use information on somatic tumor-specific variants to direct cancer treatment. A significant challenge in tumor molecular profiling is identifying tumor-specific variants in the presence of germline variants which are also identified during tumor testing. Most germline variants are benign changes not contributing to the cancer occurrence, although rare germline cancer predisposition variants may also be identified during the testing of tumor tissue. To identify true somatic tumor-specific variants, a common approach is the sequencing of both tumor and normal tissue (often peripheral blood), with variants from each tissue source used to classify variants as either somatic or germline. However paired tumor-normal testing leads to increasing costs due to the need to test both tissue sources. In addition, paired tumor-normal testing may identify potentially unwanted incidental germline cancer predisposition variants. Ideally, a solution is needed that can improve the identification of somatic tumor-specific variants obtained from NGS testing of tumor tissue only, without the need to sequence normal tissue for comparison to germline variants. This case study will show you:

- How UHN has developed a custom variant filtration strategy in Alissa Interpret to improve the identification of somatic tumor-specific variants in tumor-only testing, removing the need to sequence a reference sample.
- How building an internal knowledge base in Alissa Interpret can aid in somatic germline variant assessment.

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Alissa Interpret is a USA Class I Exempt Medical Device, Europe CE IVD, Canada and Australia Class I IVD Device.

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