Integration of gene expression profiling and artificial intelligence into personalized diagnostics for improved patient care

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Introduction and Background: The Pathway from Clinical Sample to Prognostic Risk Score

Transformative innovation in personalized medicine should be beneficially disruptive without the need for challenging implementation, ideally intertwining with existing clinical practice. Castle Biosciences uses advanced computational approaches to improve patient care by determining diagnoses and prognoses from patient samples at the pathologist's office directed for standard analysis or storage that may eventually be discarded. With this approach, Castle Biosciences developed the DecisionDx®-Melanoma prognostic test by using its expertise in molecular biology to take advantage of a long-standing clinical practice – namely, the use of formalin-fixed paraffin-embedded (FFPE) tissue for histopathological evaluation of suspicious tissue. Access to the DecisionDx-Melanoma test does not change the current standard of care for either the biopsy method or pathology processing.

Classical Pathology Methods for Melanoma Samples

After biopsy of a pigmented skin lesion suspicious for melanoma, the sample is preserved as an FFPE block, allowing a histotechnologist to cut

thin sections of tissue and mount them onto glass slides for pathologic analysis. These slices of tissue are assessed by a pathologist or specialized dermatopathologist in a variety of ways, beginning with stains such as hematoxylin and eosin (H&E) to visualize cellular and gross tissue structural abnormalities under the light microscope. Definitive determination of the risk of recurrence for patients with early-stage disease is not always possible; for these cases, Castle Biosciences developed molecular biology-based assays and tools for deeper analysis.

Pathology by Molecular Biology Techniques

While microscopic visualization and analysis by pathologists is an important step in the diagnosis and determination of prognosis, other analytes such as RNA extracted from this same tissue can provide additional insights. Over the past 20 years, FFPE tissue intended for diagnosis has also been found useful for interrogating extracted RNA to map out the complex processes contributing to elevated risk of metastasis from a patient's tumor. Castle Biosciences developed and validated innovative qRT-PCR assays to generate gene expression data that are analyzed by custom algorithms to predict the behavior of tumors by coupling the gene expression results with patient outcomes.[29,30] Castle Biosciences has mastered its discovery process, leading to the successful commercial launch of multiple prognostic and diagnostic tests that are clinically available to aid physicians and help them inform their patients (**Figure 1**).

INSET 1

A Brief History of Castle Biosciences

Medical literature contains numerous reports of discordance in the pathological review of tumor features that lead to inaccurate diagnosis of disease and incorrect staging, resulting in less precise patient management decisions.[1–3] These inaccuracies and the negative impacts on patient management strategies are exacerbated for patients who are diagnosed with early-stage and/or rarer tumors (e.g., uveal melanoma or thymoma). Diagnostic applications for less-prevalent cancers are often not as well studied or developed as those for highly funded malignancies like breast, prostate, or colorectal cancers.[4]

Castle Biosciences was founded in 2008 on the idea that analyzing the underlying molecular biology of a tumor can improve upon diagnostic and prognostic determinations based solely on clinical and pathological features. From its inception, Castle has focused on the development, validation, and application of molecular gene expression profiling (GEP) technologies for improved diagnosis and prognosis for diseases with unmet clinical need, with the goal of enhancing patient outcomes.

While the process of quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) for measuring the levels of gene expression (amount of RNA being produced in a cell) is well recognized, the innovative application of qRT-PCR to dermatologic skin cancers enabled Castle Biosciences to establish itself as one of the leaders in this field. Identifying genes that are differentially expressed in neoplastic cells and the surrounding stroma from patients with a favorable outcome, compared with those with an unfavorable outcome, provides the opportunity to utilize biomarkers of cellular transformation for improving diagnostic and prognostic precision. Two decades ago, this concept was most notably implemented in the field of breast cancer, where the 21-GEP test, OncotypeDX® (Genomic Health), was applied clinically to identify the likelihood of response to chemotherapy.[5]

Test Development and Clinical Study Design

We adhere to several foundational principles in test development for improving patient care through more informed clinical decision making. First, ensure that the unmet clinical need is clearly defined. As described above for patients with melanoma, the clinical hurdle is identifying those with apparent early-stage disease who are genuinely at high risk of recurrence. Next, determine the appropriate specimens and data sources for discovery and development. Retrospective cohorts are often used in oncology for prognostic biomarker development, as these cohorts provide documented outcomes of interest that are typically of higher value to validate the results. However, not all retrospective

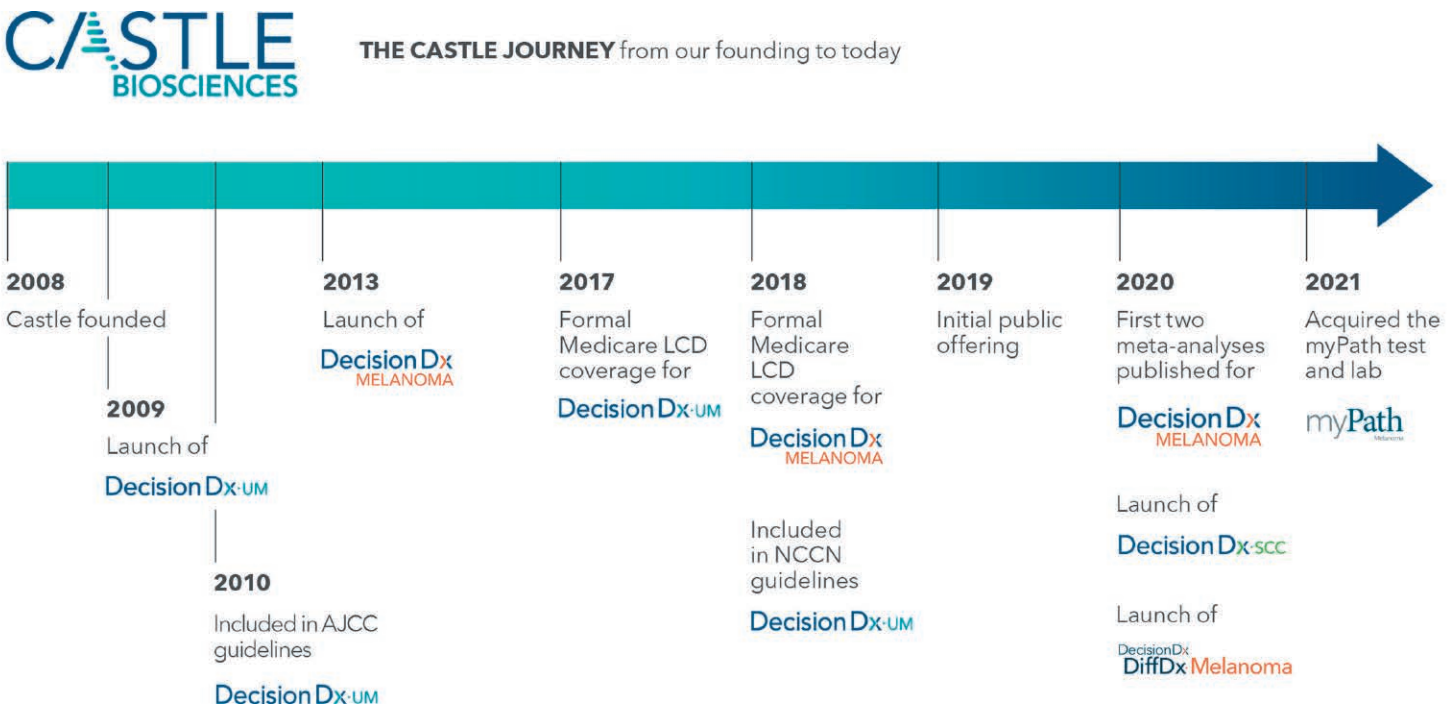

Figure 1: Major achievements along the Castle Biosciences timeline including clinical test launches, adoption into standard guidelines, and commercial milestones. AJCC, American Joint Committee on Cancer; NCCN, National Comprehensive Cancer Network.

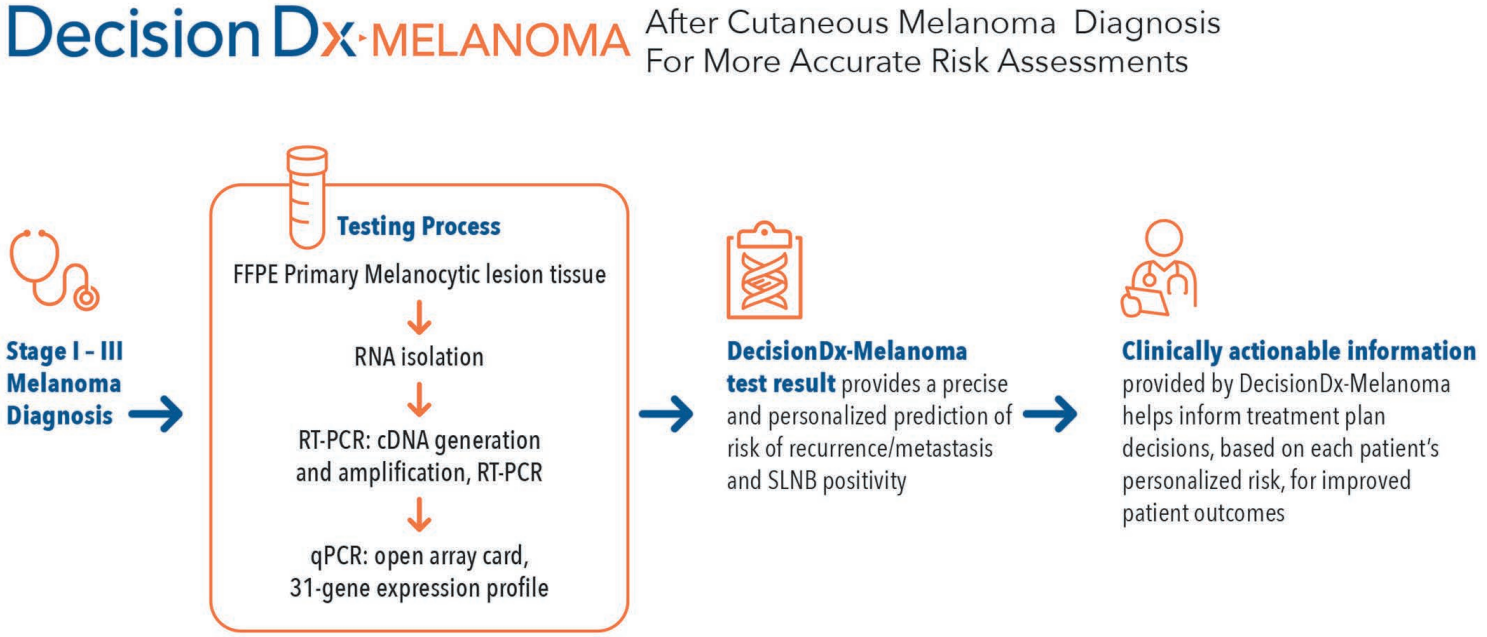

Figure 2: The DecisionDx-Melanoma 31-gene expression profile test workflow for patients with a diagnosis of Stage I-III melanoma to predict individualized risk of recurrence and sentinel lymph node biopsy positivity. cDNA, complementary DNA; FFPE, formalin-fixed paraffin-embedded; RT-PCR, reverse transcription polymerase chain reaction; SLNB, sentinel lymph node biopsy.

data are created equal, and numerous gaps are typically encountered during the data collection process. While the industry standard is to verify 20-50% of the data collected during monitoring,[31–33] Castle Biosciences has required complete monitoring of clinical data for all studies performed to date. During the review process, our in-house clinical research team verifies that information entered by collaborating institutions aligns with actual patient medical records, a critical step for ensuring successful test design and implementation.

Development of Custom Algorithms

Computational methods are employed throughout the analysis pipeline, from quality control assessment of the raw data, normalization, and final sample scoring. GEP assays rely on the development of a computational model derived

INSET 2

Uveal and Cutaneous Melanoma (UM/CM) in Focus

Over a decade ago, Castle adopted GEP technology to improve the care of patients with uveal melanoma (UM)6 and cutaneous melanoma (CM).[7,8] Castle Biosciences' path to becoming a leader in melanoma diagnostics began with a collaboration with Dr. William Harbour, a pioneer in the field of UM. UM is a rare ocular tumor that is diagnosed in approximately 2,000 people annually in the U.S.[9] Dr. Harbour's laboratory at Washington University (St. Louis) identified a panel of 15 genes (12 prognostic and 3 control genes) that could be used to accurately determine the risk of metastasis for patients diagnosed with UM, thus enabling the implementation of risk stratification-based treatment plans.[6]

Castle licensed the technology as **DecisionDx®-UM**, developed the operating procedures in a College of American Pathologists (CAP)-accredited, Clinical Laboratory Improvement Act (CLIA)-certified laboratory and completed numerous studies required for commercialization and widespread clinical use. Validation included performance studies confirming the accuracy of the early work performed in Dr. Harbour's lab, as well as clinical use studies showing that the clinicians who treated this rare condition used the **DecisionDx-UM** test to implement risk-stratified treatment plans (**Figure 1**).[6,10–13]

Like UM, CM is a disease for which current staging based on clinical and pathologic factors alone does not provide complete certainty about a patient's individual risk of recurrence or disease-specific death, particularly for those with early stage I or II CM.[14–16] Tools for improved risk stratification of stage I or II disease are a particular clinical need because these patients are presumed to have a low risk of recurrence from a population-based perspective, yet many tumors diagnosed as stage I or II eventually recur after excision. Overall, more patients from these groups die than patients with stage III disease.[17,18]

To improve the accuracy of risk stratification-based treatment plans, Castle scientists evaluated gene expression data across a range of melanoma stages to identify those that were associated with metastasis. Although the prognostic test would not be clinically applied to either *in situ* (non-invasive) or stage IV melanoma, the evaluation of data from the full gamut of stages was important for reflecting the spectrum of biologically based risk associated with CM. Once a gene panel was identified (including both control and prognostic gene targets), a training set of melanoma cases with clearly documented outcomes was randomly selected as the basis for the test. Since locking the 31 genes with the initial training set, these critical features of the **DecisionDx®-Melanoma** test have not been modified.[8] The stability of the testing platform since **DecisionDx-Melanoma** became clinically available 8 years ago has allowed for its validation in more than 4,000 research cases to date, in prospective and retrospective studies reported in over 20 peer-reviewed publications. Additional studies to assess clinical utility increased that number to over 30 articles supporting the use of the test to inform patient management. Collectively, these reports demonstrate the independent prognostic information provided by the DecisionDx-Melanoma test and the improved accuracy of risk prediction after inclusion of the GEP result (**Figure 2**).

Building on this work, Castle Biosciences is continually developing a variety of molecular tools integrating artificial intelligence (AI)-driven algorithms for diagnosis, prognosis, and better patient management in skin cancers and inflammatory dermatologic skin conditions. Castle also has a pipeline program that includes development of a GEP test designed to predict response to systemic therapies for patients with moderate-to-severe psoriasis, atopic dermatitis, and other related diseases.

from a set of training cases with known outcomes or classes, from which the model parameters are determined. New cases can then be applied to the trained model to generate a prediction of the outcome or level of risk for that case. The GEP assays are then validated for broad applicability against a set of new, independent cases from which the initial validation metrics are calculated by comparing the known outcome to the prediction made by the model.

In practice, once the appropriate specimens have been identified, the gene expression information has been attained, and all clinical data has been verified, the pieces are in place to develop a computational algorithm that can distinguish between different disease states or risk profiles. The algorithm – and the training set of specimens and data used to generate the algorithm – must be locked or fixed prior to validation using an independent cohort or test set. While other models have been derived with simple regression,[34] we have generally found that assessment of biological complexity is greatly enhanced by the use of more complicated AI modeling for accurate prediction. Upon validation of the algorithms, computational analyses of gene expression data in the tumor yield patterns that can be synthesized to generate a practical prognostic classification.

Identifying Discriminating Candidate Genes

Identification of an initial list of candidate genes is performed by pooling information from unbiased gene expression data from RNA sequencing or microarrays from clinical samples (performed in-house and mined from publicly available datasets) and through the manual addition of published genes thought to drive recurrence or metastasis. Using machine learning, the DecisionDx-Melanoma test was developed based on the expression of 28 genes (with 3 control genes) involved in a variety of biological processes such as proliferation, migration, transcriptional regulation, and keratin and melanin biogenesis (**Table 1**).

After testing multiple AI approaches, a radial basis kernel function algorithm was selected.[7,8] The radial basis function provides a high dimensional similarity metric between the samples and the training data, effectively comparing new samples to training samples in the same neighborhood of gene expression. The DecisionDx-Melanoma test reports a continuous risk assessment score that is binned to form a class call. The test was designed to include any form of metastasis (including nodal spread) as a positive case. The accuracy of the DecisionDx-Melanoma test was confirmed for the prognostication of recurrence,

Table 1: Discriminant genes in the DecisionDx®-Melanoma gene expression profile

Gene	Name	Biological functions
ARG1	Arginase 1	Cellular metabolism
TYRP1	Tyrosine related protein 1	Cellular metabolism Melanogenesis
MGP	Matrix Gla protein	Chemokine/secreted molecules
SPP1	Secreted phosphoprotein 1	Chemokine/secreted molecules Migration/chemotaxis/metastasis
KRT14	Keratin 14	Cytokeratin
KRT6B	Keratin 6B	Cytokeratin
BTG1	BTG anti-proliferation factor 1	Differentiation/proliferation
CRABP2	Cellular retinoic acid binding protein 2	Differentiation/proliferation
SPRR1B	Small proline rich protein 1B	Differentiation/proliferation
TRIM29	Tripartite motif containing 29	Differentiation/proliferation Transcriptional regulation
DSC1	Desmocollin 1	Gap junction/cellular adhesion
GJA1	Gap junction protein alpha 1	Gap junction/cellular adhesion
PPL	Periplakin	Gap junction/cellular adhesion
TACSTD2	Tumor associated calcium signal transducer 2	Gap junction/cellular adhesion
LTA4H	Leukotriene A4 hydrolase	Lymphocytic invasion
AQP3	Aquaporin 3 (Gill blood group)	Membrane transport
BAP1	BRCA1 associated protein 1	Migration/chemotaxis/metastasis Differentiation/proliferation
CLCA2	Chloride channel accessory 2	Migration/chemotaxis/metastasis
CST6	Cystatin E/M	Migration/chemotaxis/metastasis
ROBO1	Roundabout guidance receptor 1	Migration/chemotaxis/metastasis
S100A8	S100 calcium binding protein A8	Migration/chemotaxis/metastasis Differentiation/proliferation
S100A9	S100 calcium binding protein A9	Migration/chemotaxis/metastasis Differentiation/proliferation
CXCL14	C-X-C motif chemokine ligand 14	Migration/chemotaxis/metastasis Chemokine/secreted molecules
ID2	Inhibitor of DNA binding 2	Transcription regulation
RBM23	RNA binding motif 23	Transcription regulation
SAP130	Sin3A associated protein 130	Transcription regulation
EIF1B	Eukaryotic translation initiation factor 1B	Translation regulation

distant metastasis, and melanoma-specific death in multiple validation studies.[35–38]

Incorporating Gene Expression to Enhance Clinical Utility

Once a disease-specific test is validated as an independent prognostic tool, additional clinical features like histopathological staging can be incorporated for added value. Recently, we have employed AI to generate a neural network model which integrates the continuous GEP score with other available clinical data to provide an individualized risk of sentinel lymph node (SLN) positivity for each individual patient (**Figure 3**). Studies were implemented to validate its use in predicting SLN positivity, in addition to risk stratification. The association between the DecisionDx-Melanoma test result and SLN positivity was initially made from subset analyses of data from clinically tested cases. It was recognized that T1-T2* patients over 55 years of age with a Class 1A GEP result (lowest risk) had a rate of SLN positivity that was less than 5% (the cutoff traditionally associated with low risk of positivity).[39] The significant association of the DecisionDx-Melanoma risk score with SLN positivity has been validated in an independent cohort of more than 1,600 cases.[19] This integrated 31-GEP, or i31-GEP, improves upon the standard process of binning patient risk into stage groups that are traditionally used to guide treatment recommendations.

Ultimately, the value of a prognostic or diagnostic test is demonstrated by its combined clinical validity, analytic validity, and clinical utility. Clinical validity reflects the ability of the test to accurately predict the diagnosis or outcome and often requires confirmation in multiple independent cohorts. The DecisionDx-Melanoma gene set and algorithm have not changed since its validation study was completed in 2014, and performance has been reproduced in numerous multi-center prospective and retrospective cohorts.[8,36,38,40–44] Castle Biosciences has also demonstrated the independent value beyond staging through precision and accuracy across its portfolio of prognostic tests.[45–47] See **INSET 4** for Case Study.

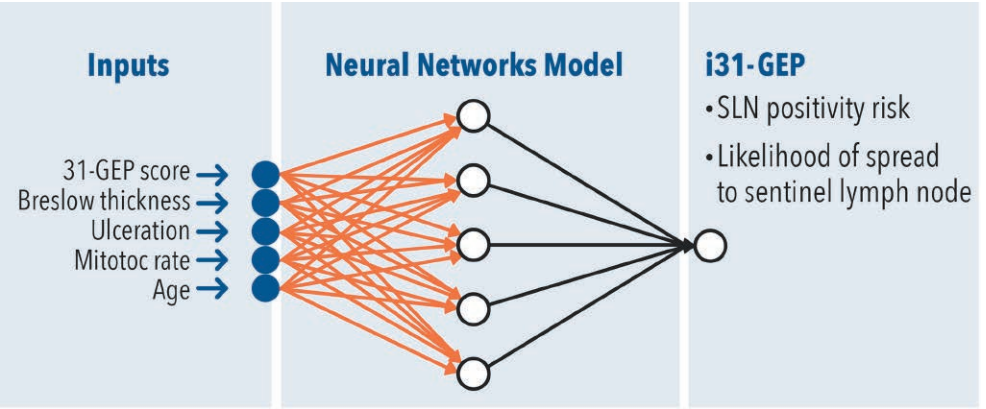

Figure 3: The integrated or i31-GEP combines the DecisionDx-Melanoma score with clinical and pathologic features (inputs) through a neural networks model to determine the likelihood of SLN positivity. GEP, gene expression profile; SLN, sentinel lymph node.

Analytic validity reflects a test's robustness and reproducibility in the clinical laboratory setting. Our diagnostic and prognostic test offerings are all performed in our CAP-accredited, CLIA-certified laboratory and are further certified by New York State standards, indicating that they meet all of the highest criteria of analytic validity.[48,49]

Finally, and most importantly, the value of a prognostic test is measured by its clinical utility, or its ability to impact patient management decisions. For melanoma, traditional risk assessment comes in the form of staging through clinicopathologic features. Consistent clinical utility studies have demonstrated that the incorporation of the DecisionDx-Melanoma test leads to changes in management for 1 out of 2 patients diagnosed with melanoma.[50–52]

The Future of Castle Biosciences: Improving Patient Care

At Castle Biosciences, we believe that when precision and accuracy meet actionability, patients benefit from improved decision making. We have a proven track record of impactful diagnostic and prognostic tests utilizing AI-informed GEP algorithms for dermatologic and ocular tumors.

INSET 3

Commitment to Improving Patient Care

Castle's commitment to innovative improvements in patient care has been highlighted in several advances over the last 2 years. New AI-driven approaches have integrated the output from the **DecisionDx-Melanoma** test with clinicopathologic features of CM tumors for personalized determination of both the risk of recurrence and the likelihood of sentinel lymph node (SLN) biopsy positivity (**Figure 3**).[19] Developments have also reached outside of CM to provide risk assessment for patients with cutaneous squamous cell carcinoma (SCC), a disease for which the risk of metastasis is generally low, yet, in total, more patients die each year from SCC than from melanoma.[20] To improve the identification of SCC patients at high risk for metastasis, the 40-gene **DecisionDx®-SCC** test was developed. Validation studies demonstrated the independent prognostic information provided by **DecisionDx-SCC** and the improvement over the most impactful staging systems currently in use.[21,22]

More recently, the **DecisionDx® DiffDx™-Melanoma** 35-GEP test has been developed and validated for clinical use.[23,24] The test is designed to improve the diagnosis of melanocytic lesions, providing more accurate classification of the 300,000 pigmented lesions suspicious for melanoma identified each year in the U.S. that are labeled as having "unknown metastatic potential" following pathological assessment. Through a strategic expansion, the **myPath® Melanoma** diagnostic test[25,26] was acquired from Myriad Genetics in May 2021 after the 2020 launch of Castle's **DecisionDx DiffDx-Melanoma** (**Figure 1**). These two complementary tools are now offered together as part of a Comprehensive Diagnostic Offering (CDO) that leverages the strengths of both **myPath Melanoma** and **DecisionDx DiffDx-Melanoma** to provide a highly accurate, objective result to aid dermatopathologists and dermatologists in characterizing difficult-to-diagnose melanocytic lesions. Castle's CDO has greatly improved the reporting of clinically actionable results.[27]

In all, the diagnostic and prognostic tests currently offered by Castle Biosciences could impact the care of over 600,000 patients with diseases of the skin. Additionally, Castle has recognized the value of next generation sequencing (NGS) technology and has made mutation analysis platforms available for clinical use alongside GEP. Using both RNA and genomic DNA isolated in parallel from the same sample, the assays detect critical prognostic point mutations in UM28 and CM. Application of these technologies, along with state-of-the-art techniques such as spatial patterning, is also being evaluated as a part of pipeline efforts to develop tests that will assist with the management of patients diagnosed with inflammatory skin diseases.

Castle is committed to fulfilling unmet clinical needs for patients by continually investing in a robust development pipeline that will expand the current portfolio. Ongoing efforts are continuing to broaden our research and development scope to include applications of GEP tests for inflammatory skin diseases. Currently, clinicians treating patients with psoriasis, atopic dermatitis, and other related conditions often have limited resources available to aid in the prediction of the likelihood of systemic therapy response. The power of GEP technology is being investigated to address this unmet need and help to point patients and their physicians toward the most appropriate therapy in a personalized manner, as opposed to costly and time-consuming empiric management approaches. Castle Biosciences is leading the charge in the application of novel precision medicine tools for more personalized patient care in an ever-expanding range of malignancies and inflammatory conditions. JPM

INSET 4

Case Study: Patient Benefits from DecisionDx-Melanoma

The past decade has seen practice-changing advancements in therapeutics for the treatment and prevention of metastatic disease and death from melanoma.[53] These therapies, while indeed lifesaving, are not without their costs, both to the patient (e.g., adverse effects) and the healthcare system. Advanced imaging techniques have been shown to lead to early identification of secondary events and help gauge the effectiveness of therapy, contributing substantially to improved outcomes.

In a real-world example of the clinical use of **DecisionDx-Melanoma**, a 52-year-old patient with melanoma on the right leg was referred to a general surgeon's office for discussion of an SLN biopsy. In line with the National Comprehensive Cancer Network (NCCN) guidelines for the tumor's pathological features (1.2mm Breslow depth, no ulceration), the patient had a lymph node biopsy of the right groin area, which was negative. This patient was staged as IB with a 5-year melanoma-specific survival rate of 97% (an overall favorable prognosis) and was therefore not eligible for adjuvant therapy.[54] The **DecisionDx-Melanoma** test was performed after the negative SLN biopsy due to the fact that metastasis cannot be ruled out based only on the finding of a negative lymph node. The GEP test identified this patient as having a biologically risky tumor (Class 2B) and, discordant with clinicopathologic risk assessment, was actually predicted to have a 5-year melanoma-specific survival rate of 86%.

This concerning finding (which made the patient eligible for adjuvant therapy) prompted the treating physician to refer the patient to medical oncology for high-intensity surveillance, with consideration for enrollment in a clinical trial. A PET/CT scan identified abnormal left deep cervical nodes, which were surgically removed and subsequently identified as metastases. Because of molecular prognostication and consequent identification of metastatic disease to the nodes, the patient was restaged to IIIB and treated with adjuvant ipilimumab. The added information coming from **DecisionDx-Melanoma** directly impacted the course of this melanoma patient's journey in line with the way the test was envisioned (**Figure 2**). Ultimately, a much more advanced disease state was uncovered than would have otherwise been presumed without GEP testing.

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* Melanoma lesions up 2mm Breslow thickness.

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Derek J. Maetzold, Founder, President, and Chief Executive Officer

Derek J. Maetzold founded Castle Biosciences and has served as our President and CEO and as a member of our board of directors since inception. Previously, Mr. Maetzold held leadership roles at Encysive Pharmaceuticals, Schering-Plough Corporation (now Merck), Integrated Communications, Amylin Pharmaceuticals, and Sandoz Pharmaceuticals (now a division of Novartis). Mr. Maetzold currently serves as a director of AltheaDX, the Ocular Melanoma Foundation, and IMPACT Melanoma. He has contributed to the discovery, development, and commercialization of five diagnostic and prognostic tests in cancers, has co-authored multiple scientific publications and is a co-inventor of a number of technologies at Castle Biosciences and Encysive Pharmaceuticals. Mr. Maetzold holds a B.S. degree in Biology from George Mason University and completed additional coursework at the University of Calgary Health Sciences Center and the MBA program at the University of California, Riverside.

Kristen Oelschlager, Chief Operating Officer and Senior Vice President

Kristen Oelschlager has served as our Chief Operating Officer since April 2021, previously serving as our Chief Operations Officer from August 2020 to April 2021, Senior Vice President, Clinical Operations from January 2018 to August 2020, and Vice President, Clinical Operations from 2013 to 2018. She joined the company as Executive Director of Operations in October 2008, as one of 3 initial employees. Ms. Oelschlager brought more than 15 years of experience in clinical nursing, clinical operations services, and clinical research to her position. She has successfully overseen the growth and development of Castle's laboratory and clinical research functions from early start-up to full commercial operations.

Sarah J. Kurley, PhD, Director of Evidence Development, R&D

Sarah Kurley has held the position Director of Evidence Development with Castle Biosciences since September 2020. Serving as a Senior Scientist from November 2017 to August 2020, Dr. Kurley supported evidence development for DecisionDx-Melanoma and contributed to the development and commercialization of DecisionDx-SCC. Dr. Kurley joined Castle Biosciences after a postdoctoral fellowship at Baylor College of Medicine where she identified novel therapeutic intervention strategies for metastatic triple-negative breast cancer. She completed her doctoral work in the Department of Cancer Biology at Vanderbilt University in 2012 where she was a recipient of a Lindau Fellowship and focused on cell-cell communication and the tumor microenvironment. She received a B.A. in Biological Sciences from Northwestern University where she graduated with honors. Dr. Kurley is an author of numerous scientific publications in the field of oncology.

Robert W. Cook, PhD, Senior Vice President, R&D

Bob Cook has served as Senior Vice President, Research & Development at Castle Biosciences since September 2020, previously serving various roles since joining Castle in 2011. Dr. Cook completed training as a postdoctoral fellow at Baylor College of Medicine where he focused on the genetic regulation of rare ovarian granulosa cell tumors. He completed his doctoral work in Biochemistry, Molecular Biology, and Cellular Biology at Northwestern University, with a focus on the structural characteristics of protein hormones important for regulating the reproductive system. Prior to pursuing his doctoral degree, Dr. Cook spent 5 years at Gen-Probe, Inc., using the company's proprietary nucleic acid amplification technology to design diagnostic assays for hematologic malignancies and solid tumors. He received a B.S. degree in Molecular Biology from Temple University in Philadelphia. Dr. Cook is an author of many medical and scientific publications and a co-inventor of several of Castle Biosciences' technologies.

Kyle R. Covington, PhD, Director of Bioinformatics, R&D

Kyle Covington has held the position of Director of Bioinformatics since February 2021, previously having the position of Senior Scientist from November 2016 to February 2021, focusing on bioinformatics, test, and evidence development for Castle Biosciences' portfolio. Prior to joining the company, Dr. Covington served as an Assistant Professor in the Human Genome Sequencing Center at Baylor College of Medicine in the Cancer Genomics group. While at Baylor, Dr. Covington contributed to many national and international cancer genomics consortiums including The Cancer Genome Atlas and the International Cancer Genome Consortium. Dr. Covington completed his doctoral work in the field of Translational Biology and Molecular Medicine at Baylor College of Medicine in 2012 where he focused on gene expression profiling and metastasis signatures in breast cancer. He received a bachelor's degree in Biology from Austin Peay State University in 2006. Dr. Covington is an author of multiple high-impact publications in the field of cancer gene expression profiling and cancer genomics.