

The purpose of this document is to provide a general product overview of the HemeScreen AML Assay. Additional information can be found on Precipio's website at www.precipiodx.com, as well as the HemeScreen® IFU (Instructions For Use) which is available upon request.

Technology Overview	HemeScreen is a proprietary set of RUO (Research Use Only) reagents used to screen the wild type (Negative) from Mutated (Positive) genes in a simplified workflow relative to alternative molecular testing technologies (RT-PCR or NGS).		
AML Assay	Acute myeloid leukemia (AML) is a clonal malignant neoplasm of myeloid cell lineage involving the blood and bone marrow, but other tissue can also be occasionally affected. In the era of personalized precision medicine, molecular changes have been used in AML classification, diagnosis, prognosis, risk stratification, and treatment.		Genes tested: <ul style="list-style-type: none"> ▪ IDH1 ▪ IDH2 ▪ FLT3 ▪ KIT ▪ CEBPA ▪ NPM1
Results	The results from HemeScreen® MPN are qualitative and DNA sequencing is required to identify specific isoforms.		
Clinical significance	<ul style="list-style-type: none"> • Mutations within the FMS-like tyrosine kinase 3 (FLT3) gene represent one of the most frequently identified genetic alterations that disturb intracellular signaling networks with a role in leukemia pathogenesis. FLT3 is a member of the class III receptor tyrosine kinase family that also includes platelet-derived growth factor receptor (PDGFR). • IDH1/2 mutations are heterozygous, typically involving an amino acid substitution in the active site of the enzyme in codon 132. The mutation results in a loss of normal enzymatic function and the abnormal production of 2-hydroxyglutarate (2-HG). the IDH1 gene mutations found in CN-AML are gain-of-function mutations that result in the production of D-2-hydroxyglutarate. • Mutations in the KIT gene are the most common (15–45%) in CBF-AML. Core binding factor (CBF) is a heterodimeric protein complex involved in the transcriptional regulation of normal hematopoiesis. Mutations in CBF-encoding genes result in leukemogenic proliferative advantages and impaired differentiation of the hematopoietic progenitors. • NPM1 gene are involved in a form of blood cell cancer known as cytogenetically normal acute myeloid leukemia (CN-AML). Somatic mutations in exon 12 of the NPM1 gene. (NPM1) are the most frequent genetic abnormality in adult AML, found in approximately 35% of all cases and up to 60% of patients with normal karyotype AML. • CEBPA gene mutation is a recurring genetic change in AML patients and has a certain correlation with clinical and laboratory features. It could be reliably used as a potential marker for minimal residual disease follow up. The prognostic significance of co-existing of siCEBPA with NPM1 mutations in patients with AML-M5 subtype needs further investigation. 		
Gene Coverage	KIT Exon 9: c.1504_1509dup; p.A502_Y503dup KIT Exon 11: c.1669_1674del; p.W557_K558del c.1669_1683del; p.W557_E561del c.1669T>C; p.W557R c.1669T>G; p.W557G c.1669T>A; p.W557R c.1727T>C; p.L576P KIT Exon 13: Mutation screening of entire exon. c.1924A>G; p.K642E c.1965T>A; p.N655K KIT Exon 17: c.2446G>C; p.D816H c.2446_2447GA>AT; p.D816I c.2447A>T; p.D816V c.2459A>G; p.D820G c.2466T>G; p.N822K c.2467T>G; p.Y823D	c.1676T>A; p.V559D c.1676T>G; p.V559G c.1679T>A; p.V560D c.1676T>C; p.V559A c.1961T>C; p.V654A c.2446G>T; p.D816Y c.2458G>T; p.D820Y c.2464A>T; p.N822Y c.2466T>A; p.N822K c.2474T>C; p.V825A	IDH1 Exon 4: c.299G>A; p.R100Q c.313G>C; p.G105R c.314G>A; p.G105D c.394C>G; p.R132G c.395G>A; p.R132H c.395G>C; p.R132P IDH2 Exon 4: c.418C>G; p.R140G c.515G>T; p.R172M c.515G>A; p.R172K c.516G>T; p.R172S c.516G>C; p.R172S c.298C>T; p.R100* c.314G>T; p.G105V c.394C>T; p.R132C c.394C>A; p.R132S c.395G>T; p.R132L c.418C>T; p.R140W c.514A>T; p.R172W c.419G>A; p.R140Q c.419G>T; p.R140L Internal Tandem Duplications Internal Tandem Duplications Internal Tandem Duplications Mutations in codons 835 and 836 Mutation screening of entire exon c.860_863dup; p.W288Cfs*12
Assay specifications	<ul style="list-style-type: none"> ▪ Specificity: 100% ▪ Sensitivity: 95% ▪ LOD: 5% 		
SKU #	HS-1P-AML	1 sample pre-plated plate	
	HS-20R-AML	20-sample free-flow reagents	
Assay contents	<ul style="list-style-type: none"> ▪ Primers-Mastermix Mix ▪ Positive controls ▪ NTC ▪ Wild type 		
Storage	-20 °C		
Machine required	HRM-enabled RT-PCR (example ThermoFisher Quantstudio 3 or higher)		

Contact For any further questions please contact our technical support team at techsupport@precipiodx.com

Disclaimer *The information in this document represents the company's best understanding of the technical and regulatory landscape; however, it should not serve as any guidance to any laboratory seeking to implement HemeScreen. Laboratory managers and medical directors should seek their own information independently through their CLIA inspector and any other state and federal regulatory body available.*