POLE / POLD1 POLYMERASE MUTATION TESTING

BIOTYPE INNOVATION

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POLE/POLD1 MUTATIONS

EXONUCLEASE DOMAIN MUTATIONS OF THE POLYMERASE SUBUNITS EPSILON (POLE) AND DELTA-1 (POLD1)

Exonuclease domain mutations (EDMs) of DNA polymerases epsilon and delta-1 subunits (POLE & POLD1) can lead to impaired proofreading during DNA replication, thereby dramatically increasing the mutation rates[1]. Tumors containing mutations in POLE or POLD1 have been shown to express 15 times more neo-antigens than microsatellite instable (MSI) tumors and 100 times more neo-antigens than microsatellite stable (MSS) tumors[2]. Neo-antigens indicate the presence of tumor-infiltrating cancer-fighting T-Cells (immune system "readiness") that are silenced by PD-1 - PD-L1-interactions. Substantial evidence suggests that tumorigenesis is promoted by both somatic and germline mutations in the exonuclease domain of POLE and POLD1. In fact, POLE mutations have been identified as risk factors for colorectal and endometrial cancer[3,4].

POLE/POLD1 MUTATIONS HAVE AN ACTIVE ROLE IN THE TUMORGENESIS.

DETECTING POLE/POLD1 EDMS IN ADDITION TO MSI TO ENABLE IMMUNE CHECKPOINT THERAPY DECISIONS

MSI testing is a promising approach to determining the response to immune checkpoint inhibitors for gastrointestinal tract and endometrial tissue tumor entities[5, 6, 7]. However, detection of the MSS phenotype excludes patients from MSI-associated therapies. Studies show that somatic POLE mutations are associated with MSS and hyper-mutated phenotypes in colorectal and endometrial tumors[3, 4]. Therefore, somatic POLE EDMs may be promising candidates for the decision-making related to immune checkpoint therapy[4, 8].

COMBINED WITH THE MSI STATUS, INFORMATION ON POLE/POLD1 MUTATIONS COULD PROVIDE VALUABLE INFORMATION FOR THERAPY-RELATED DECISIONS FOR PATIENTS WITH MSS TUMORS.

REFERENCES

1 Castellucci et al, 2017: DNA Polymerase ε Deficiency Leading to an Ultramutator Phenotype: A Novel Clinically Relevant Entity: Oncologist, 22(5):497-502.
2 S. Brigs and I. Tomlinson. "Germline and somatic polymerase ε and δ mutations define a new class of hypermutated colorectal and endometrial cancers ", J. Pathol., 230: pp. 148 – 153, 2013.
3 R. Bourdais et al, "Polymerase proofreading domain mutations: New opportunities for immunotherapy in hypermutated colorectal cancer beyond MMR deficiency", Crit. Rev. Oncol. Hematol., vol. 113, pp. 242-248, 2017.
4 J.M. Mehnert et al, "Immune activation and response to pembrolizumab in POLE-mutant endometrial cancer", J. Clin. Invest., vol. 126, no. 6, pp. 2334-2340, 2016.
5 D.T. Le et al, "Mismatch-repair deficiency predicts response of solid tumors to PD-1 blockade", Science, vol. 357, no. 6349, pp. 409-413, 2017.
6 Z.R. Chalmers et al, "Analysis of 100,000 human cancer genomes reveals the landscape of tumor mutational burden", Genome Medicine, vol. 9, no. 34, 2017.
7 H. Westdorp et al, "Opportunities for immunotherapy in microsatellite instable colorectal cancer", Cancer Immunol. Immunother. vol. 65, no. 10, pp. 1249-1259, 2016.
8 J. Gong et al, "Response to PD-1 Blockade in Microsatellite Stable Metastatic Colorectal Cancer Harboring a POLE Mutation", J. Nati. Compr. Canc. Netw., vol. 15, no. 2, pp. 142-147, 2017.

MODAPLEX POLE/POLD1 MUTATION ANALYSIS KIT

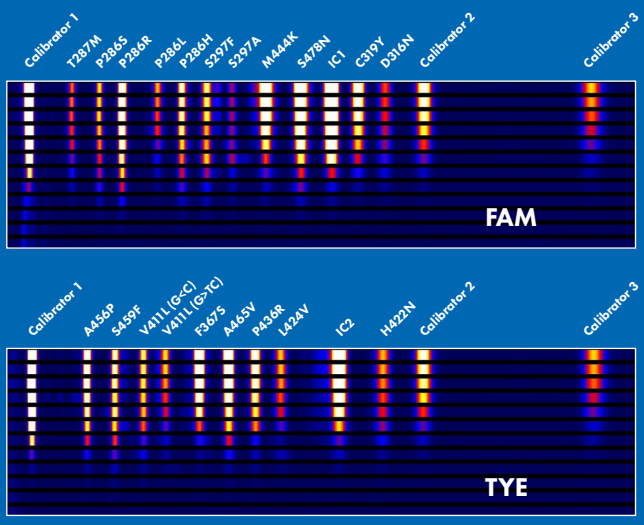
MODAPLEX POLE/POLD1 MUTATION ANALYSIS KIT COMPLEMENTS THE DECISION MAKING TO THERAPEUTIC USE IN COMBINATION WITH MSI

IDENTIFY GENETIC INSTABILITY BEYOND MSI

- Detect POLE/POLD1 mutations in MSS samples
- Combine MSI fragment analysis and POLE/POLD1 mutation detection in a single Modaplex run
- Determine genetic instability related to polymerase proofreading- or mismatch repair deficiency in less than 5 hours

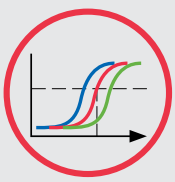
APPLY LOW SAMPLE AMOUNTS

- Tested on archived FFPE derived from colorectal and endometrial cancer tissue
- Overcome limitations on FFPE material
- Optimized input DNA amount of 4 ng



DETECT AND DIFFERENTIATE 20 POLE/POLD1 MUTATIONS

- Detection of 17 POLE EDMs
- Detection of 3 POLD1 EDMs
- Ct value-based display of positive results



ORDER INFORMATION

Product	Cat. no.
Modaplex POLE/POLD1 Mutation Analysis Kit	BTI-C003-C1-2-0050
Modaplex MSI Analysis Kit	BTI-C002-E1-2-0050

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POL BC 01 V1 EN
07/2018