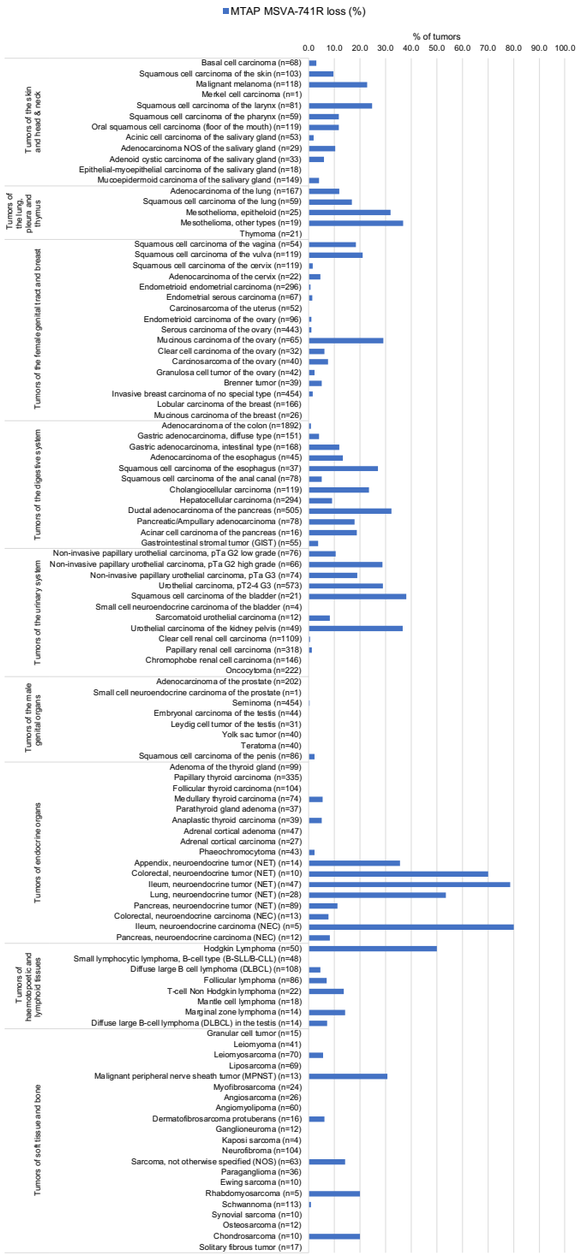
MTAP deficiency in cancer



comparison of antibodies

The antibody MSVA-741R has been validated by Gorbokon et al. (1) on 76 different normal tissue types (608 samples) according to the guidelines of the *International Working Group of Antibody Validation* (IWGAV) by comparison with a different independent antibody (2).

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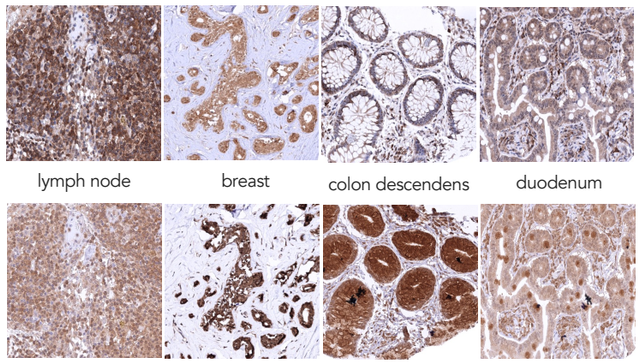

Validation Antibody

Using MSVA-741R, a distinct nuclear and cytoplasmic MTAP staining was seen in interfollicular lymphocytes of a lymph node, breast glandular cells, as well as epithelial cells of the colon, and in the epithelium of the duodenum. Using the validation antibody, a highly similar MTAP staining pattern was observed in lymph node, the breast and most other tissues. A strong additional staining of mucus producing goblet cells was only seen by the validation antibody in the mucosa of the colon and the duodenum. These stainings were considered an antibody specific cross-reactivity of the validation antibody.

(2) Uhlen, M., Bandrowski, A., Carr, S. *et al.* A proposal for validation of antibodies. *Nat Methods* 13, 823–827 (2016).

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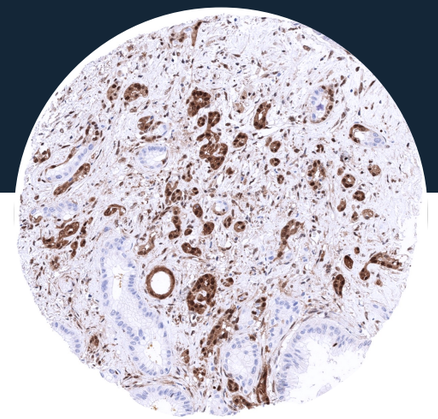
M T A P

clone MSVA-741R

Sensitive and specific marker for homozygous 9p21 deletions



Publication Summary

Prevalence of S-methyl-5'-thioadenosine Phosphorylase (MTAP) Deficiency in Human Cancer: A Tissue Microarray Study on 13,067 Tumors From 149 Different Tumor Types

Gorbokon et al. Am J Surg Pathol. 2024 Oct 1;48(10):1245-1258.

MS
Validated Antibodies

Prevalence of S-methyl-5'-thioadenosine Phosphorylase (MTAP) Deficiency in Human Cancer: A Tissue Microarray Study on 13,067 Tumors From 149 Different Tumor Types

Gorbokon et al. Am J Surg Pathol. 2024 Oct 1;48(10):1245-1258. (1)

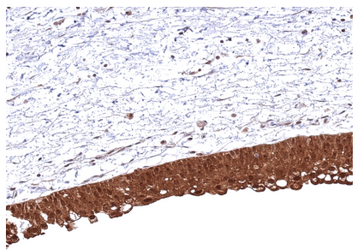
The ubiquitously expressed S-methyl-5′-thioadenosine phosphorylase (MTAP), coded by the MTAP gene at 9p21, is often homozygously deleted in cancer. Homozygous deletion of the MTAP gene results in a complete MTAP expression loss (MTAP deficiency) which causes critical vulnerability of affected cancer cells towards drugs targeting multiple different pathways. IHC detection of MTAP expression loss can be used as a marker for neoplastic transformation in many tissue types (1).

The analysis of 13'067 tumors by Gorbokon et al. provides a comprehensive catalogue on MTAP deficiency in human cancer. MTAP expression loss occurred in 83 of 149 tumor categories.

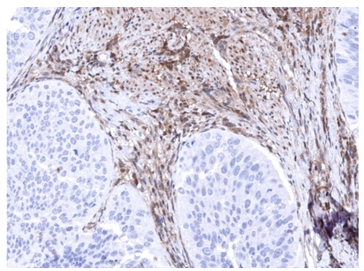
Key Findings

MTAP deficiency was most common in neuroendocrine neoplasms, Hodgkin's lymphoma, mesothelioma, bilio-pancreatic adenocarcinomas, urothelial neoplasms, squamous cell carcinomas, and in various types of sarcomas.

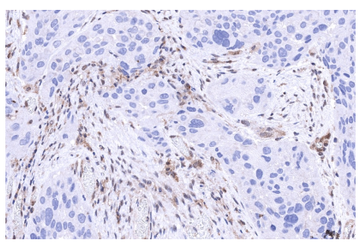
In most tumor types, homozygous 9p21 deletion was the cause of MTAP expression loss in 90% to 100% of cases. Exception: MTAP deficiency was not due to deletion in neuroendocrine tumors, Hodgkin's and other lymphomas.



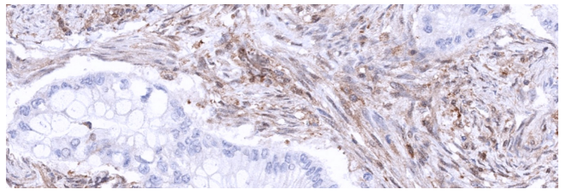
Urothelium with intense cytoplasmic and nuclear MTAP staining of all cells.



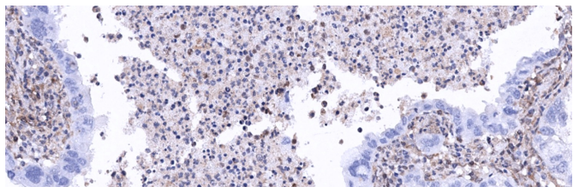
Non-invasive urothelial carcinoma (pTa) lacking MTAP staining in all tumor cells. MTAP positive stroma cells serve as an internal control.



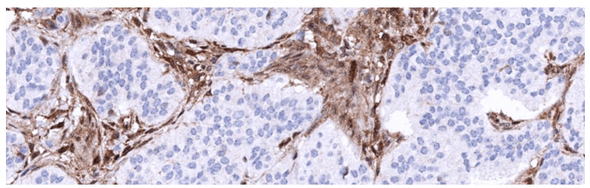
Urinary bladder - invasive urothelial carcinoma lacking MTAP expression.



Uterus, cervix – Adenocarcinoma lacking MTAP staining in tumor cells



Stomach – Gastric adenocarcinoma (intestinal type) without MTAP staining in tumor cells.



Appendix – Neuroendocrine tumor with complete absence of MTAP staining in tumor cells

Conclusion

MTAP IHC has very high specificity and sensitivity for detection of homozygous 9p21 deletion involving MTAP.

MTAP expression loss is a useful marker for neoplastic transformation in many tissue types (mesothelium, urothelium, pancreas, lung, others) (1).

Ranking order

The prevalence of MTAP deficiency is shown in a ranking list below (data from Gorbokon et al. (1) summarized in own graphics).