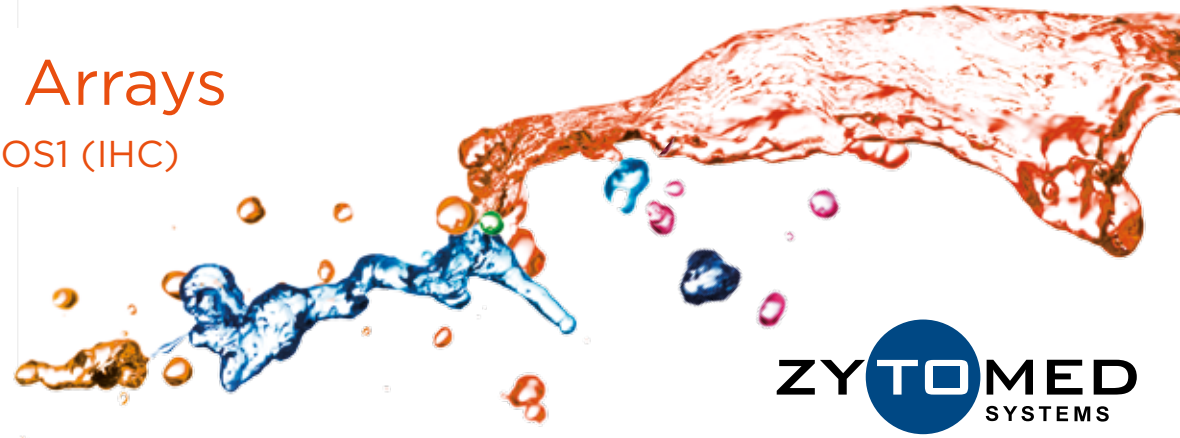
Cell Control Arrays

Cell Control Block ROS1 (IHC)



Cell Control Block ROS1 (IHC)

for the establishment, validation and quality control of ROS1 immunohistochemistry

ROS1 is a receptor tyrosine kinase (TK) with structural similarity to the anaplastic lymphoma kinase (ALK) protein. ROS1 translocations define a subset of patients with non-small cell lung carcinoma (NSCLC). About 1–2 % of NSCLC cases have a ROS1 rearrangement leading to overexpression of a chimeric ROS1 protein with constitutional TK activity, resulting in unregulated cell growth [1]. Clinical studies and case reports show that treatment with tyrosine kinase inhibitors such as crizotinib and ceritinib represents an effective therapeutic strategy in patients with activating ROS1 rearrangements [2,3].

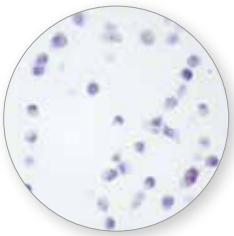
Due to the low incidence of ROS1 translocations, a screen with anti ROS1 antibodies on NSCLC tissue sections is often performed, followed by confirmatory FISH analysis of ROS1 positive tissue.

A number of studies have shown a good correlation between ROS1 FISH and ROS1 IHC with reported sensitivities of 94% to 100% and specificities of 76 %–100%. The different results obviously depend, at least in part, on the cut-offs used to determine positivity [4-6]. ROS1 IHC tests have several pitfalls which could lead to false positive results. EGFR-mutant tumors can show strong staining as well as mucinous adenocarcinomas which show a more granular staining pattern. Positive staining can occur on reactive pneumocytes, alveolar macrophages and giant cells.

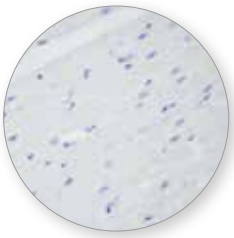
Due to the subjective interpretation of staining intensities and inter-observer variability of ROS1 IHC, an additional FISH or a molecular analysis is recommended in weak or focal cases, especially in medical facilities with less experienced physicians [6].

The establishment of a ROS1 immunohistochemistry as well as its routine use in diagnostics requires a validated process using appropriate controls [4]. The Cell Control Array ROS1 (IHC) block serves as a positive control for the detection of ROS1 protein in lung and other tissues. It is a homogenous paraffin block including two ROS1 positive cell lines, one ROS1 negative cell line, and one core of heart muscle tissue. The two positive ROS1 cell lines differ in their level of ROS1 expression, showing weak and medium expression, respectively. In addition, the Cell Control Array ROS1 can be used for the detection of mRNA of a CD74-ROS1 fusion using real-time PCR.

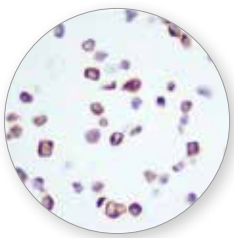
The small size of the control block sections allows for simultaneous mounting of patient material sections and control block sections on the same slide. Thus, you will have an on-slide control array staining (OSCAR) proving a regular stain even after years of storage.



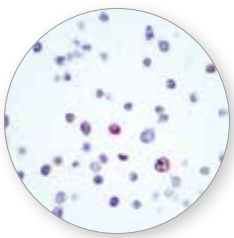
negative



Heart muscle



ROS1 medium



ROS1 low

Protocol

- Pre-treatment in EDTA-Buffer (ZUC029-500), 35 min, steamer
- ROS-1, clone D4D6 (Cell Signaling Technology)
- Dilution 1:100 for 60 minutes at RT
- Polymer detection Kit POLHRP-100 (25 min / 30 min)
- DAB High Contrast (DAB500PLUS) 10 min

Product information

Description	Form	Volume	Cat. No.
Cell Control Array ROS1 (IHC)	1 Block	2 ROS1 positive cell lines, 1 ROS1 negative cell line, 1 core of heart muscle tissue	MB-CC ROS1

Bibliography

[1] Uguen A, de Brakeleer M. ROS1 fusions in cancer: a review. Future Oncol 12:1911-1928, 2016

[2] Mazières J *et al.* Crizotinib therapy for advanced lung adenocarcinoma and a ROS1 rearrangement: results from the EUROS1 cohort. J Clin Oncol 33:992-999, 2015

[3] Shaw AT *et al.* Crizotinib in ROS1-rearranged non-small-cell lung cancer. N Engl J Med 371:1963-1971, 2014

[4] Bubendorf L *et al.* Testing for ROS1 in non-small cell lung cancer: a review with recommendations. Virchows Arch 469:489-503, 2016

[5] Selinger CI *et al.* Screening for ROS1 gene rearrangements in non-small-cell lung cancers using immunohistochemistry with FISH confirmation is an effective method to identify this rare target. Histopathology 70:402–411, 2017

[6] Luk P *et al.* Biomarkers for ALK and ROS1 in Lung Cancer. Arch Pathol Lab 142: 922-928, 2018

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