

**p62/KEAP1/NRF2 Pathway Antibody
Sampler Kit**
Orders: 877-616-CELL (2355)
orders@cellsignal.com

Support: 877-678-TECH (8324)

Web: info@cellsignal.com
cellsignal.com

1 Kit (7 x 20 microliters)

3 Trask Lane | Danvers | Massachusetts | 01923 | USA

For Research Use Only. Not for Use in Diagnostic Procedures.

Product Includes	Product #	Quantity	Mol. Wt	Isotype/Source
SQSTM1/p62 (D1Q5S) Rabbit mAb	39749	20 µl	62 kDa	Rabbit IgG
Phospho-SQSTM1/p62 (Ser349) (E7M1A) Rabbit mAb	16177	20 µl	62 kDa	Rabbit IgG
LC3A/B (D3U4C) XP® Rabbit mAb	12741	20 µl	14, 16 kDa	Rabbit IgG
KEAP1 (D6B12) Rabbit mAb	8047	20 µl	60-64 kDa	Rabbit IgG
NRF2 (D1Z9C) XP® Rabbit mAb	12721	20 µl	97-100 kDa	Rabbit IgG
HO-1 (E3F4S) Rabbit mAb	43966	20 µl	28 kDa	Rabbit IgG
NQO1 (D6H3A) Rabbit mAb	62262	20 µl	29 kDa	Rabbit IgG
Anti-rabbit IgG, HRP-linked Antibody	7074	100 µl		Goat

Please visit cellsignal.com for individual component applications, species cross-reactivity, dilutions, protocols, and additional product information.**Description**

The p62/KEAP1/NRF2 Pathway Antibody Sampler Kit provides an economical means of detecting the non-canonical mechanism of NRF2 activation involving autophagy. The kit includes enough antibodies to perform two western blot experiments with each primary antibody.

Storage

Supplied in 10 mM sodium HEPES (pH 7.5), 150 mM NaCl, 100 µg/ml BSA, 50% glycerol and less than 0.02% sodium azide. Store at -20°C. *Do not aliquot the antibodies.*

Background

The cap 'n' collar (CNC), leucine zipper (bZIP) transcription factor NRF2 (also called nuclear factor erythroid 2-related factor 2 (NFE2L2)) is the master regulator of the cellular antioxidant response, regulating the expression of over 200 genes that contain antioxidant response elements (AREs) in their regulatory regions by heterodimerizing with small MAF proteins (1). While NRF2 is expressed in all cell types, its basal protein levels are usually kept low during homeostatic conditions, mainly by KEAP1 (Kelch-like ECH-associated protein 1). Under normal conditions, KEAP1 binds to and targets NRF2 for ubiquitination-dependent proteasomal degradation. Upon oxidative stress, KEAP1 is modified on some sensor cysteines, affecting its conformation and thus interfering its binding to NRF2, allowing newly synthesized NRF2 to accumulate and translocate to the nucleus to activate its target genes, including HO-1 (heme oxygenase 1) and NQO1 (NAD(P)H:quinone oxidoreductase 1) (2,3). Another mode of NRF2 regulation involves the autophagy adapter protein p62 (or sequestosome 1 [SQSTM1]) in a KEAP1-dependent but cysteine-independent manner, the so called non-canonical pathway. Autophagy is a tightly regulated cellular quality control system that removes damaged proteins or organelles. Autophagy can also be activated to degrade macromolecules to provide nutrients under cellular starvation stress. p62, especially upon phosphorylation at Ser349 (Ser351 in mouse p62), can compete with NRF2 for binding KEAP1 and, as a result, p62 sequesters KEAP1 into the autophagosome and prevents KEAP1-mediated NRF2 degradation. This process may also require autophagy protein LC3. In addition, studies also found that KEAP1 is a p62-regulated substrate for autophagy-mediated degradation, indicating that p62 also plays a role in controlling KEAP1 turnover (4,5). Dysregulation of autophagy results in prolonged NRF2 activation and this may contribute to many diseases, including cancer and neurodegenerative diseases (6-9).

Background References

1. Zhu, M. and Fahl, W.E. (2001) *Biochem Biophys Res Commun* 289, 212-9.
2. Bellezza, I. et al. (2018) *Biochim Biophys Acta Mol Cell Res* 1865, 721-33.
3. Yamamoto, M. et al. (2018) *Physiol Rev* 98, 1169-203.
4. Jiang, T. et al. (2015) *Free Radic Biol Med* 88, 199-204.
5. Nezis, I.P. and Stenmark, H. (2012) *Antioxid Redox Signal* 17, 786-93.
6. Rojo de la Vega, M. et al. (2018) *Cancer Cell* 34, 21-43.
7. Sánchez-Martín, P. et al. (2019) *FEBS J* 286, 8-23.
8. Shah, S.Z.A. et al. (2018) *Front Mol Neurosci* 11, 310.
9. Ichimura, Y. and Komatsu, M. (2018) *Front Oncol* 8, 210.

Trademarks and Patents

Cell Signaling Technology is a trademark of Cell Signaling Technology, Inc.

All other trademarks are the property of their respective owners. Visit cellsignal.com/trademarks for more information.

Limited Uses

Except as otherwise expressly agreed in a writing signed by a legally authorized representative of CST, the following terms apply to Products provided by CST, its affiliates or its distributors. Any Customer's terms and conditions that are in addition to, or different from, those contained herein, unless separately accepted in writing by a legally authorized representative of CST, are rejected and are of no force or effect.

Products are labeled with For Research Use Only or a similar labeling statement and have not been approved, cleared, or licensed by the FDA or other regulatory foreign or domestic entity, for any purpose. Customer shall not use any Product for any diagnostic or therapeutic purpose, or otherwise in any manner that conflicts with its labeling statement. Products sold or licensed by CST are provided for Customer as the end-user and solely for research and development uses. Any use of Product for diagnostic, prophylactic or therapeutic purposes, or any purchase of Product for resale (alone or as a component) or other commercial purpose, requires a separate license from CST. Customer shall (a) not sell, license, loan, donate or otherwise transfer or make available any Product to any third party, whether alone or in combination with other materials, or use the Products to manufacture any commercial products, (b) not copy, modify, reverse engineer, decompile, disassemble or otherwise attempt to discover the underlying structure or technology of the Products, or use the Products for the purpose of developing any products or services that would compete with CST products or services, (c) not alter or remove from the Products any trademarks, trade names, logos, patent or copyright notices or markings, (d) use the Products solely in accordance with CST Product Terms of Sale and any applicable documentation, and (e) comply with any license, terms of service or similar agreement with respect to any third party products or services used by Customer in connection with the Products.

Orders: 877-616-CELL (2355) • orders@cellsignal.com • Support: 877-678-TECH (8324) • info@cellsignal.com • Web: cellsignal.com
For Research Use Only. Not for Use in Diagnostic Procedures.