

## Product Information

### Anti-BACE-2, C-terminus (501-518)

Antibody produced in rabbit, Affinity isolated antibody

Product Number **B 8060**

#### Product Description

Anti-BACE-2, C-terminus (501-518) is developed in rabbit using as immunogen a synthetic peptide corresponding to the C-terminus of human BACE-2 (amino acids 501-518), conjugated to KLH. This sequence is identical in mouse BACE-2 and is not found in the BACE-1 homologue. The antibody is affinity-purified using the immunizing peptide immobilized on agarose.

Anti-BACE-2, C-terminus (501-518) recognizes human BACE-2 (52 kDa in cells transfected with BACE-2) by immunoblotting. Staining of the BACE-2 band in immunoblotting is specifically inhibited with the BACE-2 immunizing peptide.

The amyloid- $\beta$  peptide ( $A\beta$ ) is a principal component of cerebral plaques in the brain of patients with Alzheimer's disease (AD). Formation of  $A\beta$  involves proteolytic cleavage of the  $\beta$ -amyloid precursor protein (APP) by two proteases,  $\beta$ - and  $\gamma$ -secretase.<sup>1-3</sup> Cleavage of APP by  $\beta$ -secretase leads to the generation and extracellular release of APPs- $\beta$ , a ~100 kDa soluble N-terminal fragment and intracellular C-terminal fragments (CTFs) bearing the complete  $A\beta$  domain. Cleavage of the CTFs by  $\gamma$ -secretase, leads to the formation of  $A\beta$ .<sup>3,4</sup> The membrane-associated aspartic protease BACE-1 ( $\beta$ -site APP cleaving enzyme, Asp2 or memapsin 2) has been identified as  $\beta$ -secretase.<sup>5-8</sup> A second homologue was also identified and termed BACE-2, (also termed Asp1, DRAP or memapsin 1).<sup>9-11</sup> BACE-1 and BACE-2 have similar structural organization and share 51% amino acid sequence identity. BACE-1 is highly expressed in neurons and constitutes the predominant  $\beta$ -secretase activity in human brain responsible for cleavage of APP at the  $\beta$ -cleavage site to promote  $A\beta$  production. BACE-2 is expressed in the central nervous system and in many peripheral tissues, however its expression levels in neurons is substantially lower than BACE-1.<sup>9,10</sup> The *BACE-2* gene resides on chromosome 21 in the obligate Down's syndrome (DS) region at 21q22.3.

An elevated level of BACE-2 is observed in APP trisomic brains of DS patients, suggesting that BACE-2 may play a role in DS pathology.<sup>12,13</sup> BACE-2 has also been demonstrated to cleave both wild type and Swedish mutant APP at the  $\beta$ -site in transfected cells.<sup>10,14</sup> In addition, BACE-2 also cleaves APP at secondary sites, between Phe<sup>19</sup>-Phe<sup>20</sup> and Phe<sup>20</sup>-Ala<sup>21</sup> of the  $A\beta$  region of APP.<sup>14</sup> Over expression of BACE-2 in transfected cells produces intracellular CTFs, as well as increases extracellular release of APPs- $\beta$ , but paradoxically reduces  $A\beta$  production. The reduction of  $A\beta$  formation has been attributed to the second cleavage site of BACE-2 on APP. Selective inactivation of BACE-2 by RNAi results in increased release of secreted APPs- $\beta$  and  $A\beta$  production,<sup>15</sup> suggesting a role for BACE-2 in suppressing  $A\beta$  production in cells expressing both BACE-1 and BACE-2.

#### Reagent

The antibody is provided as a solution in 0.01 M phosphate buffered saline, pH 7.4, containing 15 mM sodium azide as a preservative.

Antibody concentration: approx. 3 mg/mL

#### Precautions and Disclaimer

Due to the sodium azide content a material safety data sheet (MSDS) for this product has been sent to the attention of the safety officer of your institution. Consult the MSDS for information regarding hazardous and safe handling practices.

#### Storage/Stability

For continuous use, store at 2-8 °C for up to one month. For extended storage, freeze in working aliquots. Repeated freezing and thawing is not recommended. Storage in "frost-free" freezers is not recommended. If slight turbidity occurs upon prolonged storage, clarify the solution by centrifugation before use. Working dilution samples should be discarded if not used within 12 hours.

### Product Profile

A working concentration of 5-10 µg/ml is determined by immunoblotting using a whole extract of human HEK293 cells transfected with human BACE-2.

A working concentration of 15-30 µg/ml is determined by immunofluorescence staining of human HEK293 cells transfected with human BACE-2.

**Note:** In order to obtain best results and assay sensitivity in various techniques and preparations, we recommend determining optimal working concentrations by titration test.

### References

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