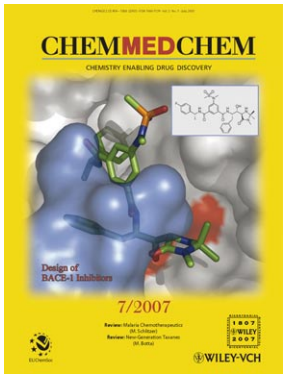
Cover Picture



James C. Barrow*, Kenneth E. Rittle, Phung L. Ngo, Harold G. Selnick, Samuel L. Graham, Steven M. Pitzenberger, Georgia B. McGaughey, Dennis Colussi, Ming-Tain Lai, Qian Huang, Katherine Tugusheva, Amy S. Espeseth, Adam J. Simon, Sanjeev K. Munshi, and Joseph P. Vacca

The cover picture shows a close-up view of a modified hydroxyethylamine aspartyl protease inhibitor bound in the BACE-1 active site. The imidazolidinone ring serves as a rigid scaffold for orienting substituents into the S1′ and S2′ sites of the enzyme while making hydrogen bond contacts to the catalytic aspartate groups (highlighted in red) and the flap (colored in blue). Based on this X-ray crystal structure, additional analogues were designed to exploit the imidazolidinone heterocycle as a template for potent BACE-1 inhibitors. For details, see the Communication by J. Barrow et al. on p. 995 ff.