Huntington’s disease (HD) is marked by a polyglutamine expansion in the disease protein huntingtin (Htt), significant neurodegeneration in several brain areas including the hypothalamus, and an eventual loss of body weight, or “wasting.” Mutant Htt with its polyglutamine expansion can associate with several proteins to form cytosolic protein aggregates. One of these is huntingtin-associated protein-1 (HAP1). A recently defined role for HAP1 in trafficking of epidermal growth factor receptor (EGFR) may provide clues to the pathology of HD. This week Li et al. report hypothalamic neurodegeneration in mutant HAP1 (−/−) mice. The HAP1 knockout mice also did not gain weight after birth, dying only a few days apparently because of the loss of feeding behavior. Terminal deoxynucleotidyl transferase-mediated biotinylated UTP nick end labeling and electron microscopy revealed cell death throughout the hypothalamus. HD mice also had degenerating neurons in the hypothalamus. The authors suggest that loss of HAP1 function in HD arises from binding to mutant Htt, and that a loss of proper EGFR signaling may underlie the behavioral phenotype seen in HD mice, and perhaps patients. HAP1 may play an important part in hypothalamic regulation of feeding behavior, the details of which may one day point to therapeutic targets for HD in humans.