Caffa I, D'Agostino V, Damonte P, Soncini D, Cea M, Monacelli F, Odetti P, Ballestrero A, Provenzani A, Longo VD, Nencioni A. (2015). Fasting potentiates the anticancer activity of tyrosine kinase inhibitors by strengthening MAPK signaling inhibition. *Oncotarget.* 20;6(14):11820-32.

Tyrosine kinase inhibitors (TKIs) are now the mainstay of treatment in many types of cancer. However, their benefit is frequently short-lived, mandating the search for safe potentiation strategies. Cycles of fasting enhance the activity of chemo-radiotherapy in preclinical cancer models and dietary approaches based on fasting are currently explored in clinical trials. Whether combining fasting with TKIs is going to be potentially beneficial remains unknown. Here we report that starvation conditions increase the ability of commonly administered TKIs, including erlotinib, gefitinib, lapatinib, crizotinib and regorafenib, to block cancer cell growth, to inhibit the mitogen-activated protein kinase (MAPK) signaling pathway and to strengthen E2F-dependent transcription inhibition. In cancer xenografts models, both TKIs and cycles of fasting slowed tumor growth, but, when combined, these interventions were significantly more effective than either type of treatment alone. In conclusion, cycles of fasting or of specifically designed fasting-mimicking diets should be evaluated in clinical studies as a means to potentiate the activity of TKIs in clinical use.