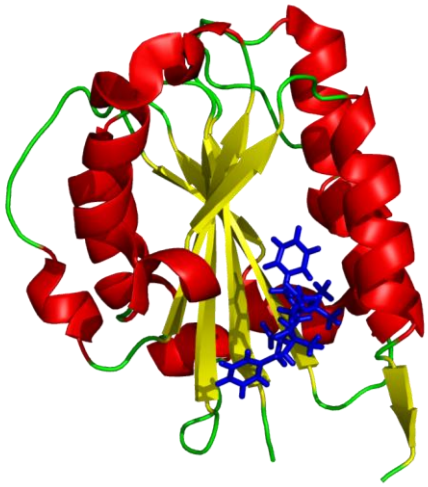
Novel antagonists in early and late stages of cancer development.

A multidisciplinary research team led by groups from CIC bioGUNE and the University of the Basque Country has developed a novel family of synthetic compounds with strong antiproliferative and antimetastatic activity in a murine model of colon carcinoma. The compounds disrupt a protein-protein interaction that mediates intercellular adhesion events that in turn promote tumor growth and metastasis in the liver.

Molecules that mimic the intercellular adhesion molecule 1 (ICAM-1) were designed as competitive inhibitors of the integrin leukocyte function associated antigen 1 (LFA-1), disrupting their interaction and inhibiting tumor growth and metastasis in mice. The structural analysis of the compound binding to the isolated I-domain of the integrin suggests that they might be allosteric inhibitors instead of competitive ones.

Nowadays, 90% of deaths from cancer are caused by metastasis from the primary tumours. Colon cancer is not among the highest mortality rate cancers, but it often develops metastasis in the liver, which it is.

This study opens the way for the future development of modified compounds with improved pharmacological properties.



The figure shows one of the compounds (in blue sticks) bound to the allosteric site of the I-domain of integrin LFA-1 (shown as a ribbon scheme with different colors for the different secondary structure elements).