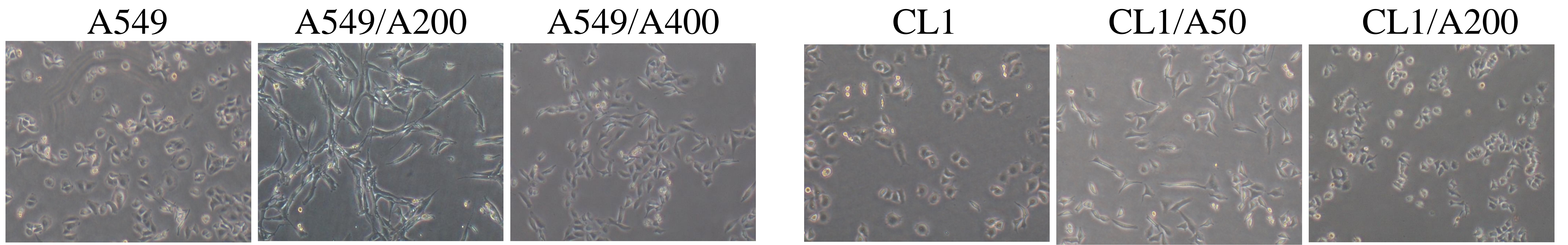
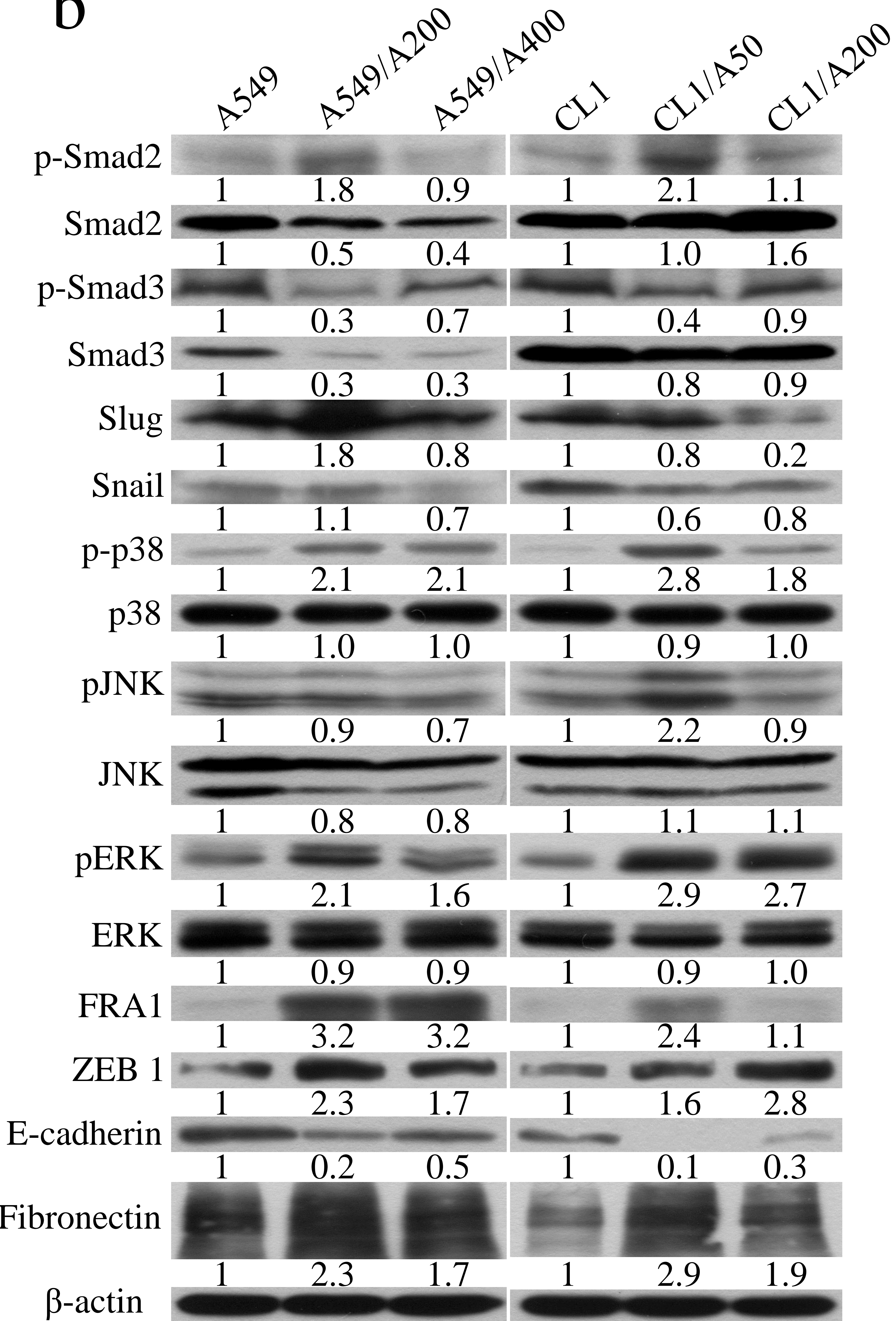


Supplementary Figure 1

a



b



Establishment of the pemetrexed resistant A549 and CL1 sublines and analysis of the pemetrexed-induced metastasis *in vitro*.

The pemetrexed resistant sublines were established from parental cells in a stepwise manner with low cellular density by exposure to increasing concentrations of pemetrexed. After several months' treatment, the colonies were formed and amplified in the presence of 25 nM pemetrexed until confluence. It required months to allow those selected cells amplified before the drug dose was increased in multiples of two for the next round of selection. The pemetrexed resistant sublines maintained at 200 nM pemetrexed are denoted as A549/A200. A similar approach was applied to obtain the CL1/A50 subline. (a) Microscopic image taken with an inverted light microscope. (b) Western blots of pemetrexed resistant sublines.