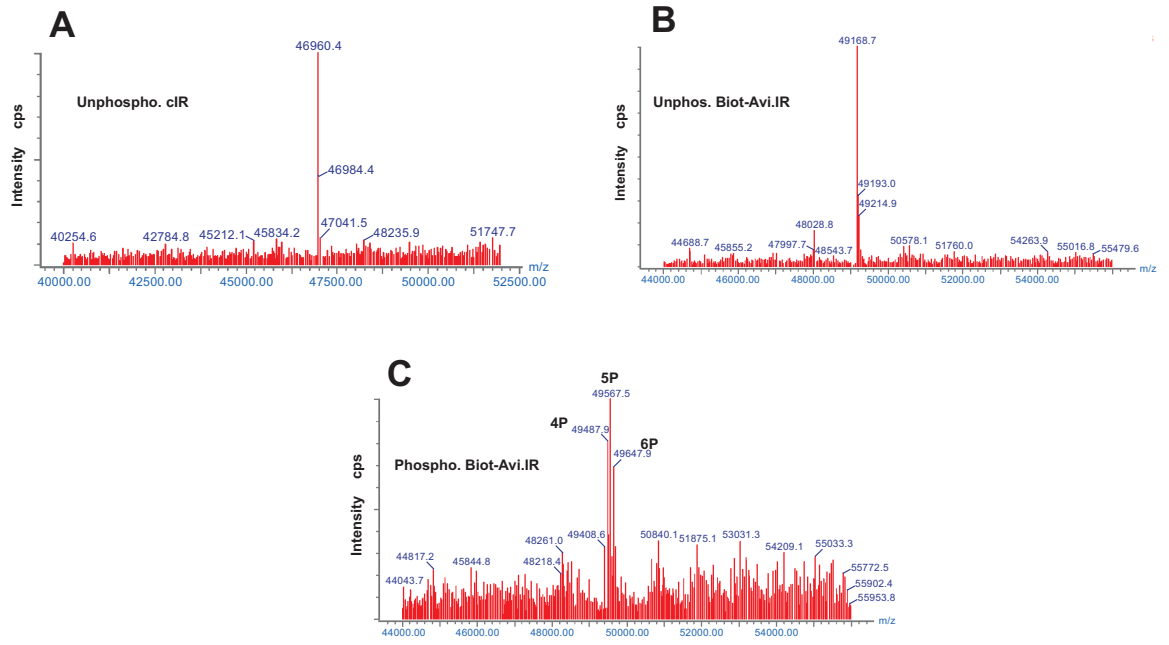

Fig. (S1). Purity of the protein preparations. The purity of unphosphorylated cIR (**A**), biotinylated Avi.IR (**B**) and biotinylated phosphorylated Avi.IR (**C**) was determined by HPLC-MS/MS, as described under 'Materials and Methods'. Representative mass spectra are represented. The theoretical molecular weights (MW_{th}) of cIR and biotinylated Avi.IR are 46962 and 49166, respectively. The biotinylated phosphorylated Avi.IR (**C**) is a mixture of proteins phosphorylated at 4 (MW_{th} = 49486), 5 (MW_{th} = 49566) and 6 (MW_{th} = 49646) sites.

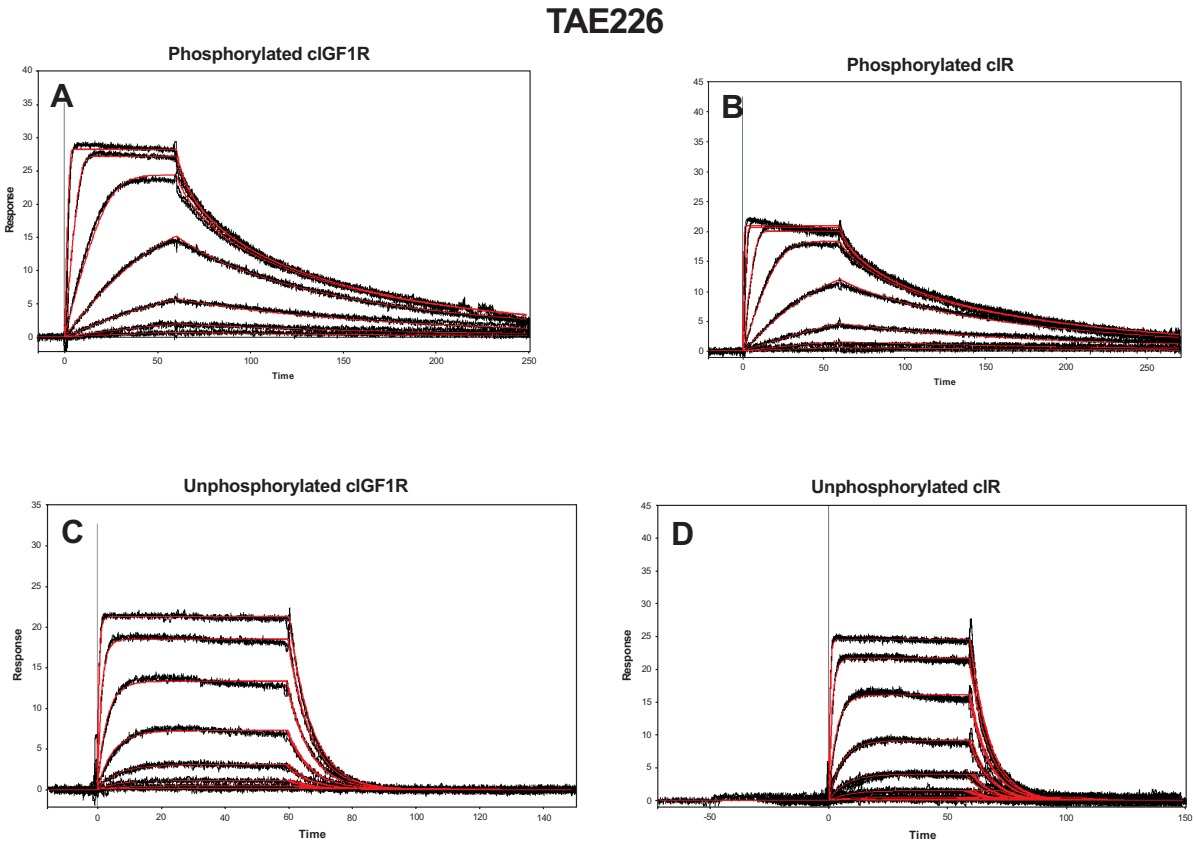

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Fig. (S2). contd….

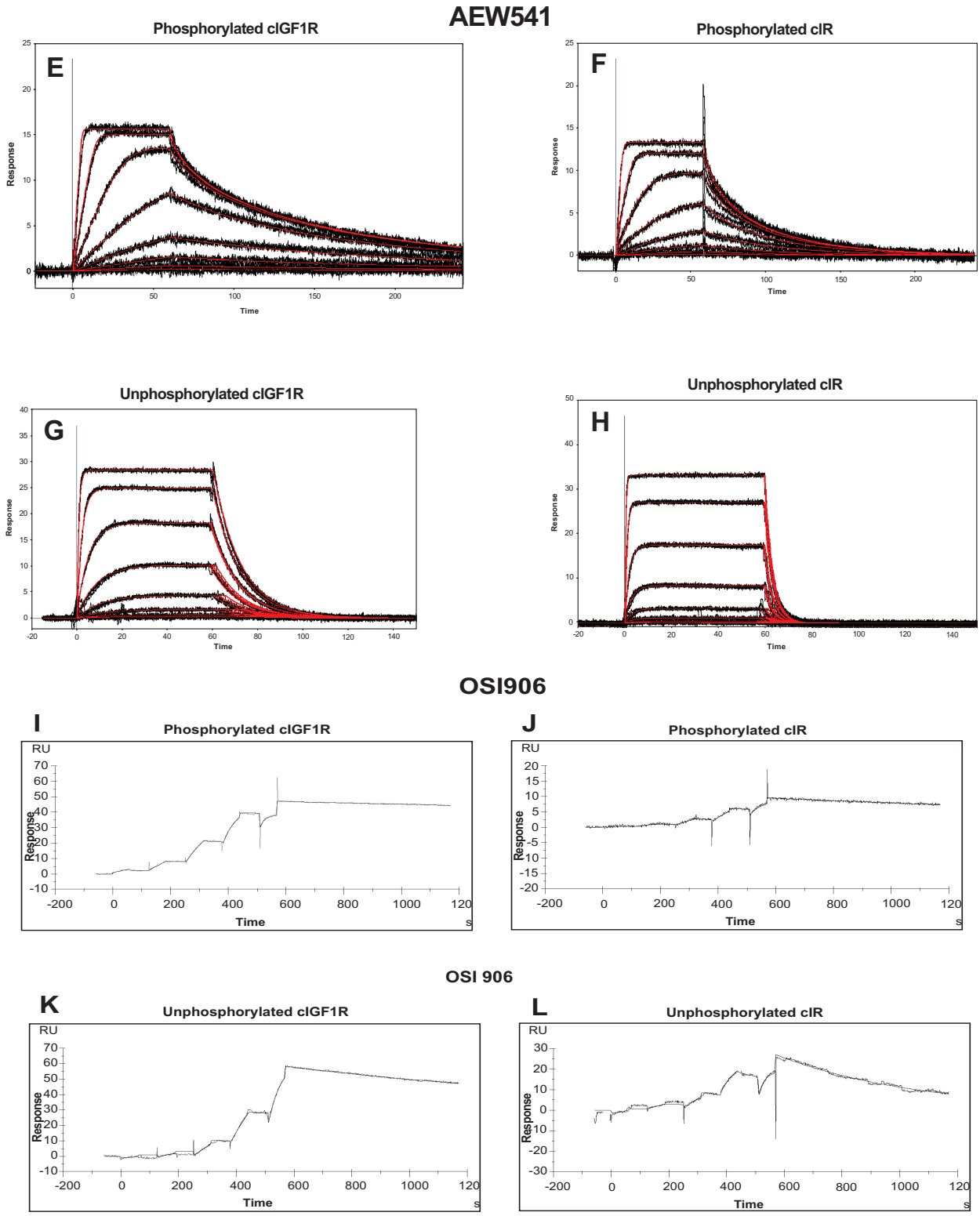

Fig. (S2). Kinetic characterization of inhibitors binding to phosphorylated and unphosphorylated biotinylated Avi.IGF1R and Avi.IR proteins. Sensorgrams obtained with TAE226 (**A**-**D**), AEW541 (**E**-**H**), OSI906 (**I**-**L**) with phosphorylated (**A, E, I**) and unphosphorylated (**C, G, K**) biotinylated Avi.IGF1R and on phosphorylated (**B, F, J**) and unphosphorylated (**D, H, L**) biotinylated Avi.IR. The TAE226 and AEW541 sensorgrams were obtained using the standard procedure. Sensorgrams for OSI906 were obtained by kinetic titration. See the legend of Fig. (**4**) for more details and under 'Material and Methods' for the kinetic titration.

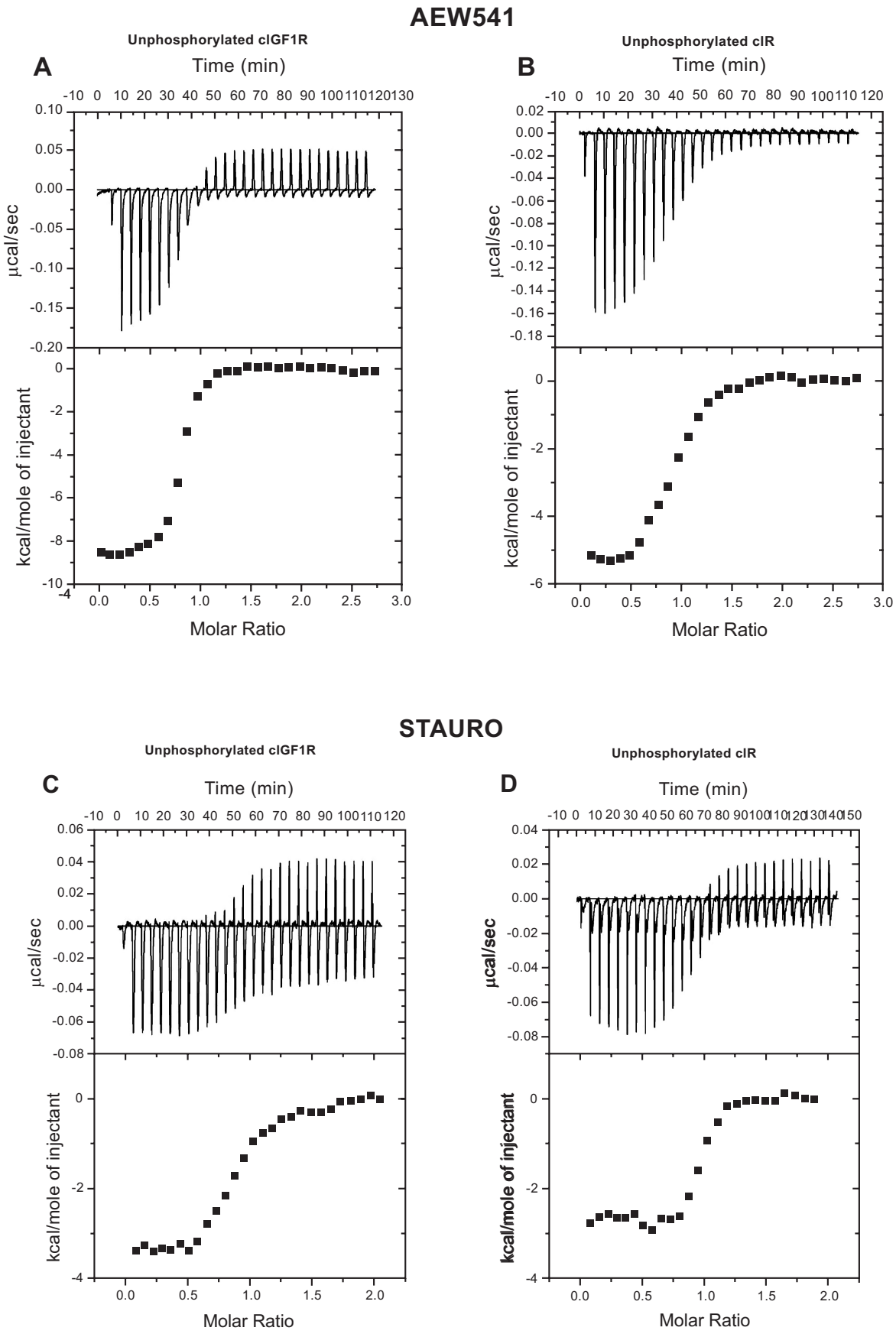
AEW541
Unphosphorylated cIGF1R
A
Time (min)
µcal/sec
kcal/mole of injectant
Molar Ratio
Unphosphorylated cIR
B
Time (min)
µcal/sec
kcal/mole of injectant
Molar Ratio
STAURO
Unphosphorylated cIGF1R
C
Time (min)
µcal/sec
kcal/mole of injectant
Molar Ratio
Unphosphorylated cIR
D
Time (min)
µcal/sec
kcal/mole of injectant
Molar Ratio

Fig. (S2). contd….

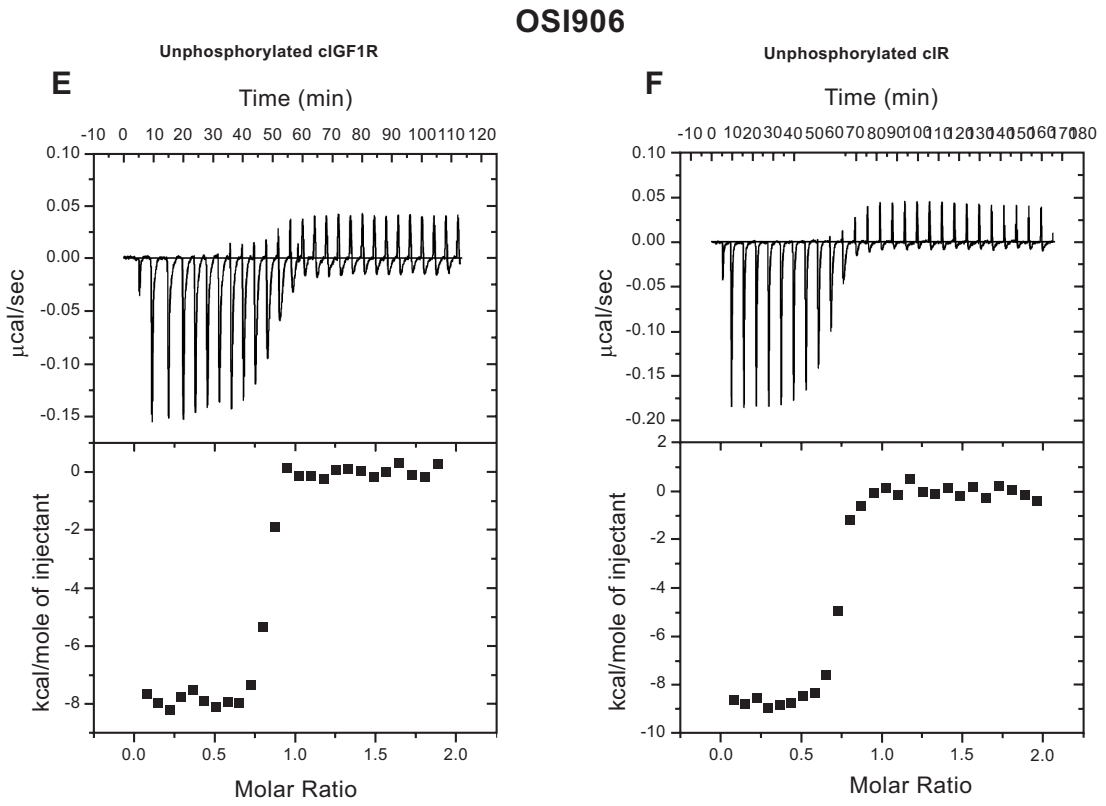

Fig. (S3). Isothermal calorimetry analysis of the interaction between the compounds and unphosphorylated IGF1r and cIR. The IGF1R (**A, C, E**) and cIR (**B, D, F**) proteins were titrated into a solution of AEW541 (**A, B**), STAURO (**C, D**) or OSI906 (**E, F**) as described under 'Material and Methods' in a VP-ITC calorimeter (Microcal). See the legend of Fig. (**5**) for more details.