



**Supplementary Figure 1.** Comparison of eight algorithms under conditions where overfitting is strictly avoided. The *i-Score1600* and *s-Biopredisi1600* scores are explained in the legend for Table 2. The observed siRNA activities in subset A831 are plotted against predicted siRNA activities by *i-Score1600* (**A**), *s-Biopredisi1600* (**B**), *Reynolds* (**C**), *Ui-Tei* (**D**), *Amarzguioui* (**E**), *Katoh* (**F**), *Hsieh* (**G**), and *Takasaki* (**H**). Continuous numeric scores given by algorithms in **A**, **B**, **F**, and **H** are evenly divided into ten ranks to enable visual comparison with ordinal or nominal scores in **C**, **D**, **E**, and **G**. Short bars indicate the mean at each rank. Dotted lines indicate 75% inhibition. Note that the *Hsieh* (**G**) and *Takasaki* (**H**) scores fail to predict siRNA activities for this dataset.