

**Supplementary Information**

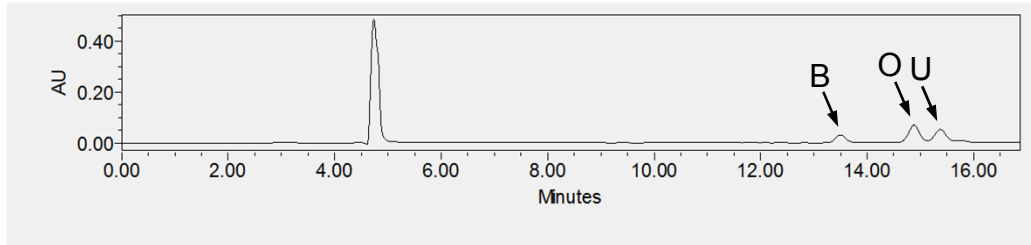
**Dual activities of the anti-cancer drug candidate PBI-05204 provide neuroprotection in brain slice models for neurodegenerative diseases and stroke**

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**Supplementary Figure S1. Relative abundance of the 3 major triterpenoid constituents of Fraction 0-4 as shown by chromatographic separation. A, Chromatogram of Fraction 0-4. B, Chromatograms of triterpene standards for oleanolic acid ("O"), ursolic acid ("U"), and betulinic acid ("B"; all purchased from Sigma) as indicated. Elution conditions were isocratic 95% MeCN with 0.1% formic acid at a flow rate of 0.6 mL/min using a Gemini C-18 column.**

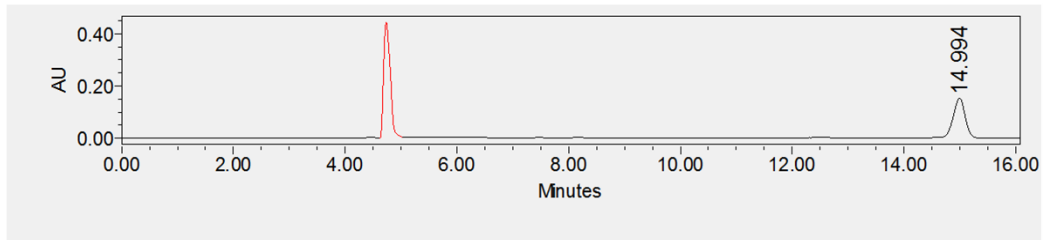
# Supplementary Figure S1

A

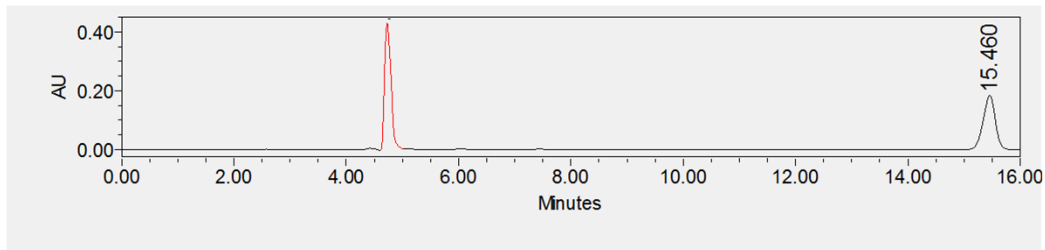


Fraction 0-4

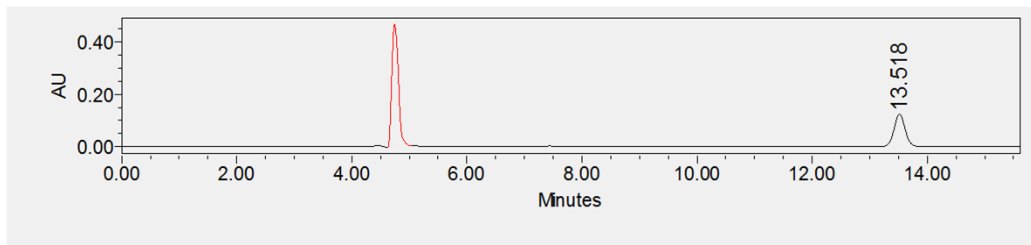
B



Oleanolic acid



Ursolic acid



Betulinic acid

**Supplementary Figure S2. Activation of ARE target genes by ursolic acid and betulinic acid.**

Activation of the ARE genes by ursolic acid and betulinic acid was examined using more closely-spaced concentration steps, showing that betulinic acid, like ursolic acid, is able to induce clear upregulation of *Srx* and *Hmox1* despite its toxicity at higher concentrations (see Fig. 5). Rat primary corticostriatal co-cultures were treated for 6 h with Fraction 0-4 (in  $\mu\text{g/ml}$ ) or ursolic acid and betulinic acid (in  $\mu\text{M}$ ) at the concentrations indicated, then harvested and processed for qPCR analysis of the ARE target genes shown. Quantitative RNA values were normalized to the *GAPDH* reference control and fold-expression changes are expressed relative to the DMSO-carrier only condition ("--") set to a value of 1. Dark blue bars denote statistically significant differences with respect to the DMSO-carrier only control by a Student's *t*-test at  $p < 0.05$ .

# Supplementary Figure S2

