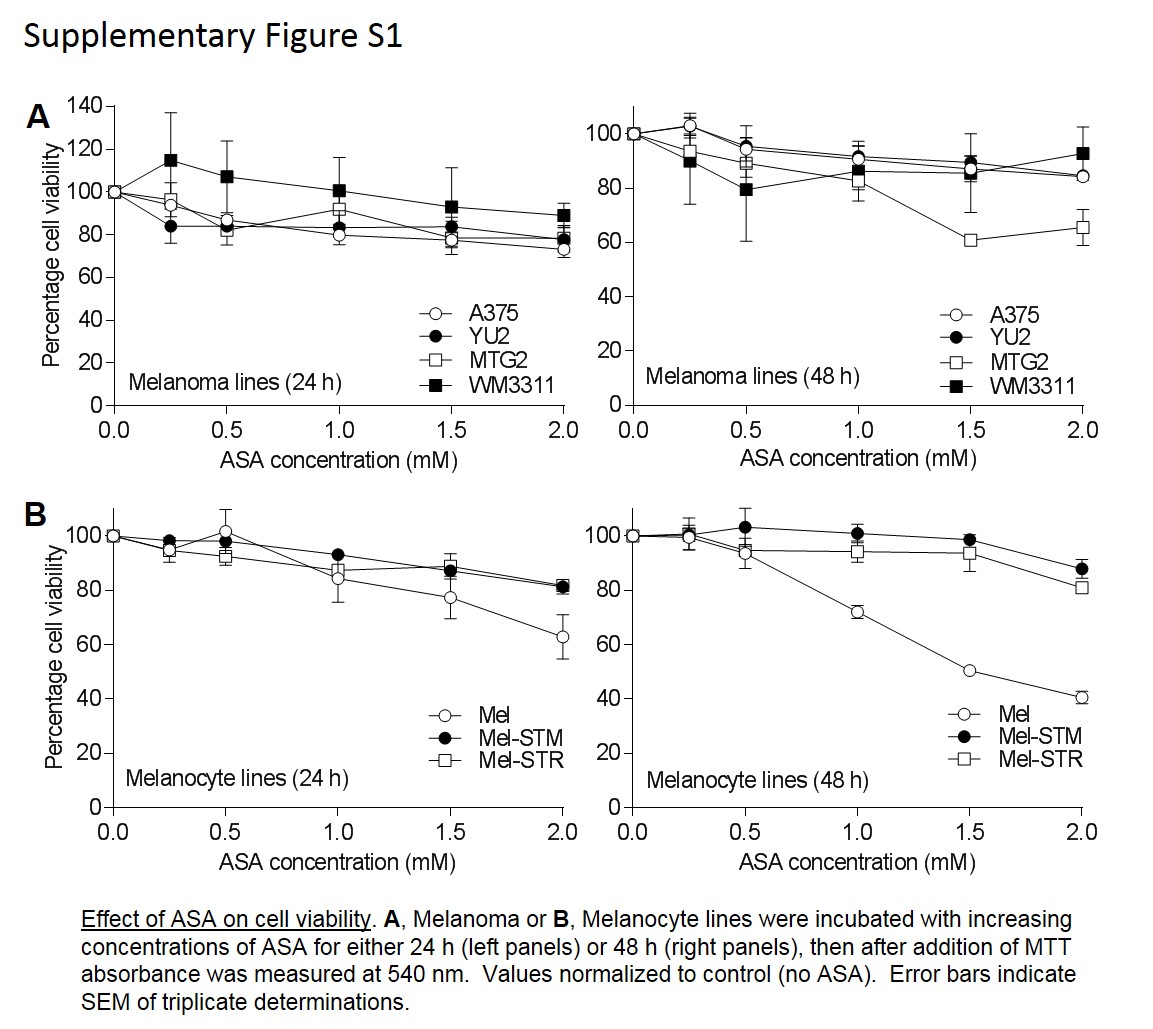
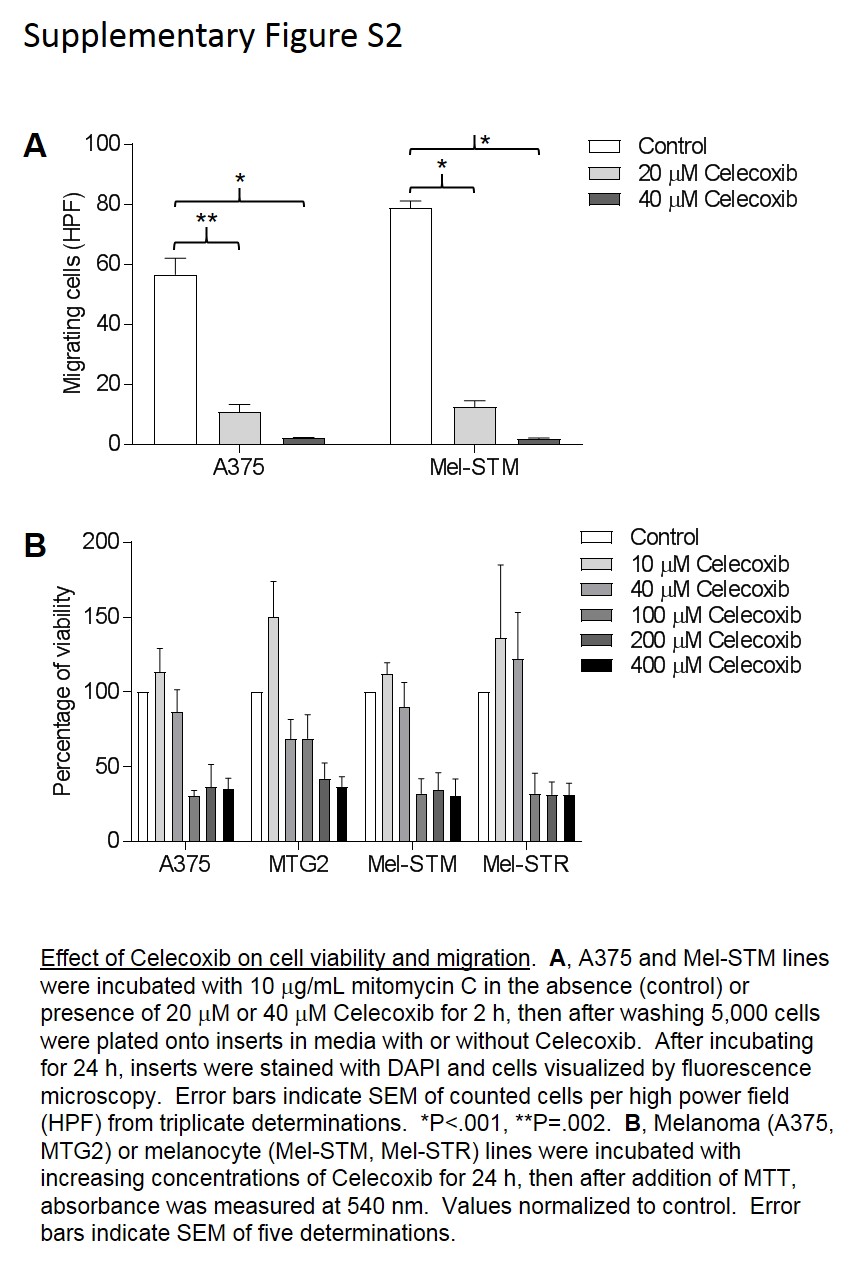
**Supplementary information**

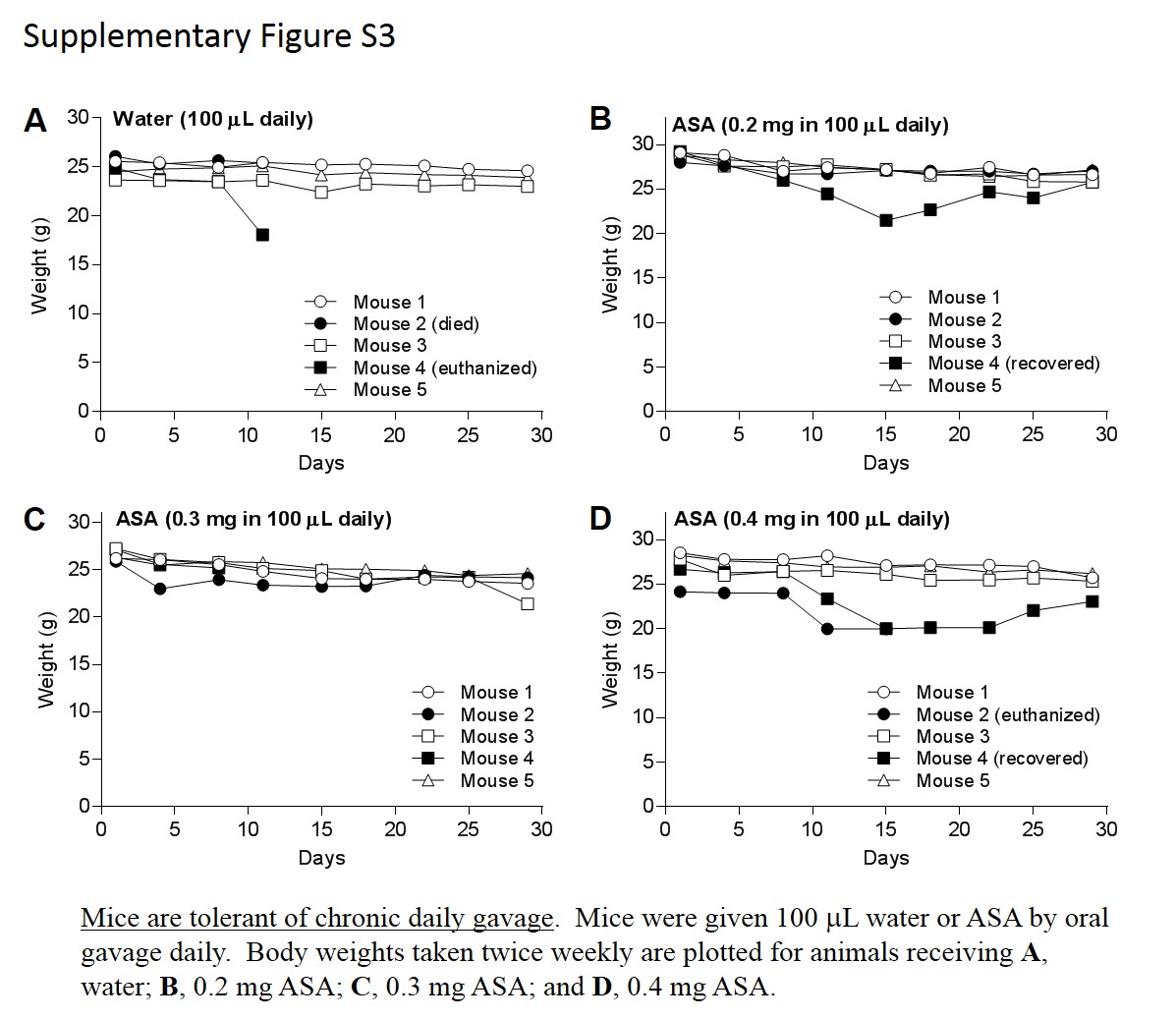
**Detection of ASA metabolites and PGE2 by liquid chromatography-mass spectrometry (LC-MS)**

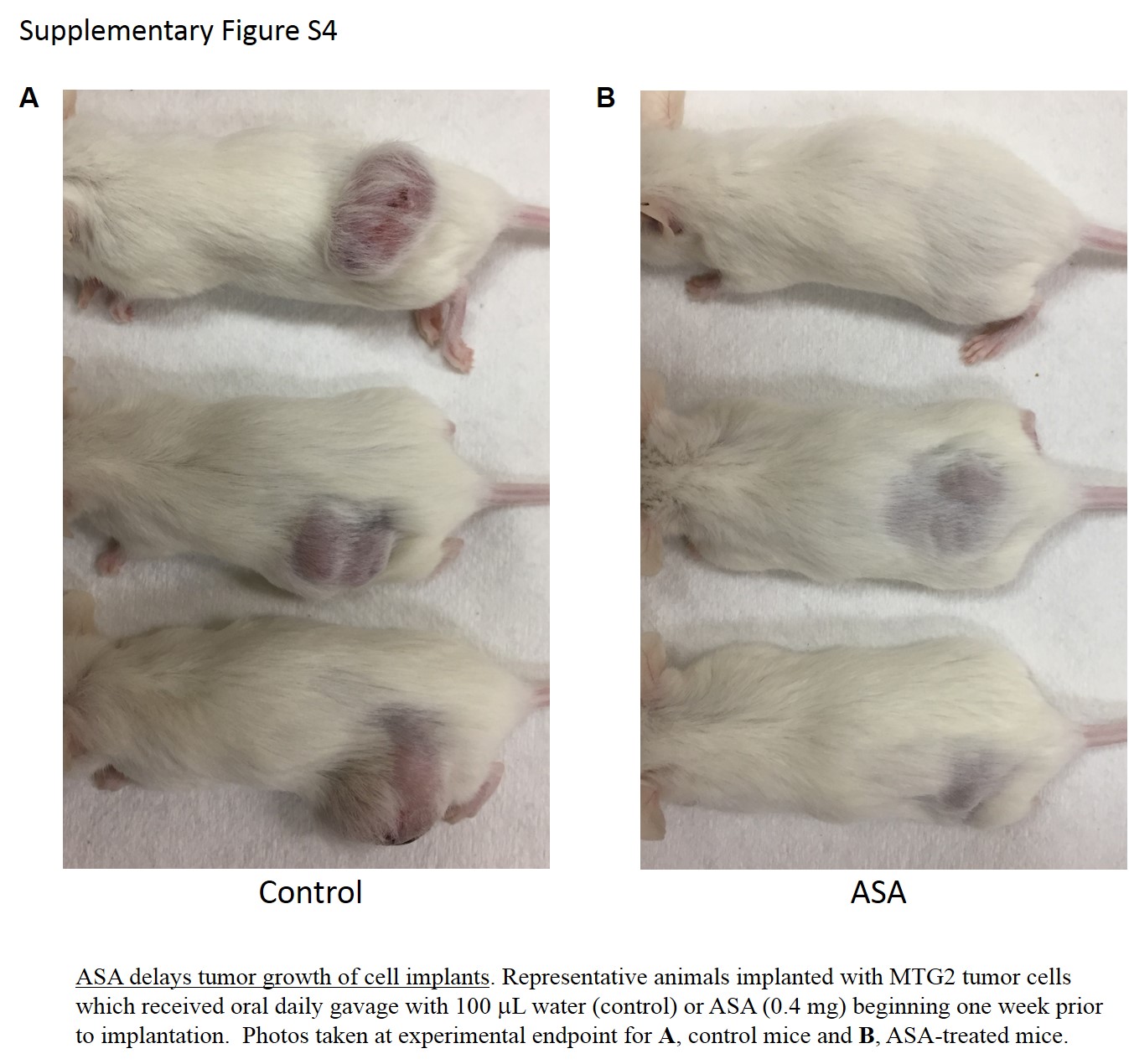
Plasma samples (50-100 L) were spiked with 20 µL of the internal standard working solution (combined solution of d4-PGE2, d3-aspirin, and d4-salicylic acid at 25 µM each, Sigma) and the following were added to prevent free radical-catalyzed peroxidation: 25 μL of 1M potassium dihydrogen phosphate buffer, 40 L of 1 M citric acid, and 5 L of 10% butylated hydroxytoluene (BHT). After vortexing, 1 mL methyl tert-butyl ether (MTBE) was added to each and samples were placed on ice for 15 min with occasional vortexing and then centrifuged for 4 min at 15,000 g at 4 °C. The organic layer was transferred into an Eppendorf tube and evaporated via speedvac. The dried extract was reconstituted in 60 μL of 35% mobile phase A (0.1% formic acid in water) / 65% mobile phase B (0.1% formic acid in acetonitrile), centrifuged and the supernatant was then transferred into auto-injector vials. Metabolites were separated on a Waters 100 x 2.1 mm CSH Phenyl-Hexyl column maintained at 30 °C and connected to an Agilent HiP 1290 Sampler, Agilent 1290 Infinity pump equipped with an Agilent 1290 Flex Cube and Agilent 6550 quadrupole time-of-flight mass spectrometer. Samples (1 µL injection volume) were analyzed in random order. The chromatography was ramped from 10% B to 50% B over 10 min, post-time was 5 min, and the flowrate was 0.3 mL per min throughout. Retention times were optimized using commercial standards, and high resolution quantitation was performed using the accurate mass of each metabolite based on peak area ratios to internal standards. Results were analyzed using the Agilent Mass Hunter Quant software package, version B.07.00.

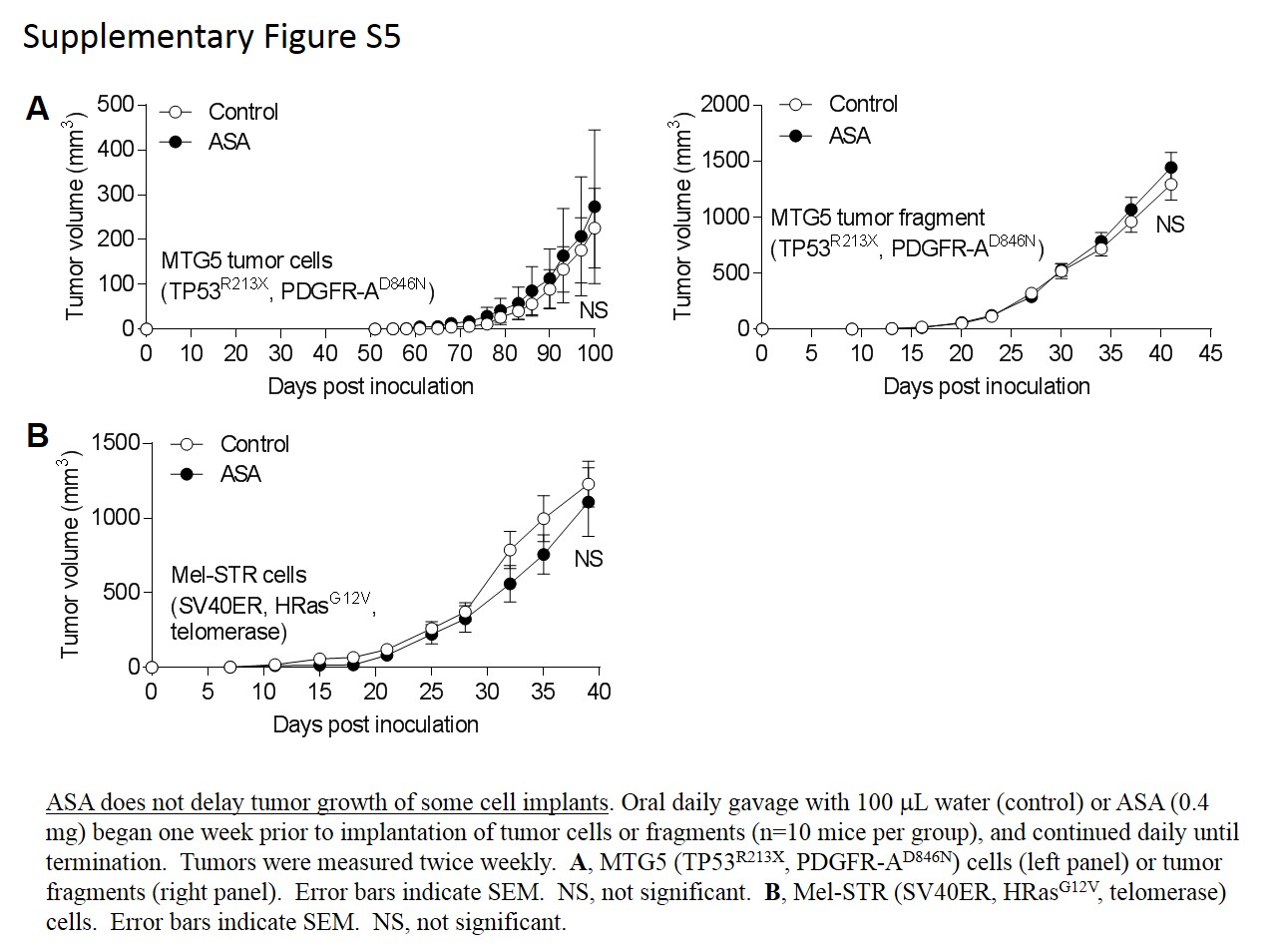
For skin samples, 20-30 mg were transferred into tared bead mill tubes (Qiagen, 1.4 mm), weights were obtained, and then 400-µL water spiked with 10 µL of the internal standards d4-PGE2 (5 µg per mL) and d4-salicylic acid (10 ng per mL) was added. Samples were treated and extracted as described above. MTBE extraction was repeated once more with the emulsion in the bead mill tube and combined with the dried organic layer. The dried extract was reconstituted in 100 µL of the mobile phase (65% B), centrifuged and the supernatant was then transferred into auto-injector vials. Metabolites were separated on an Agilent Eclipse C18 2.1 x 50 mm column and then subjected to MS as described above. Injection volume was 2 µL, with samples analyzed in random order. The chromatography was isocratic at 65% B over 4 min, post-time was 3 min, and the flowrate was 0.3 mL per min throughout. Quantitation was performed as described above.

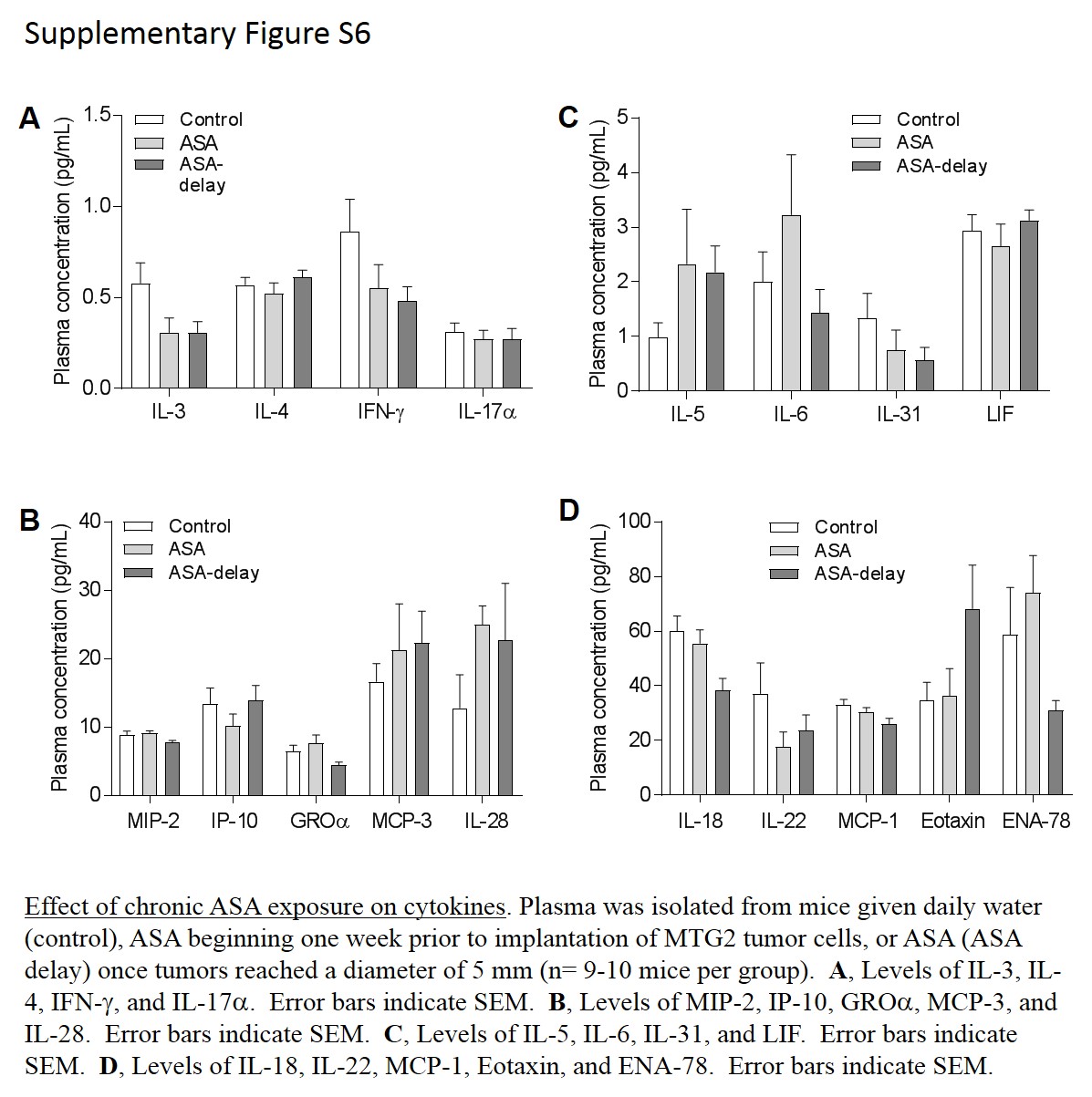
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