

## **Supporting Information**

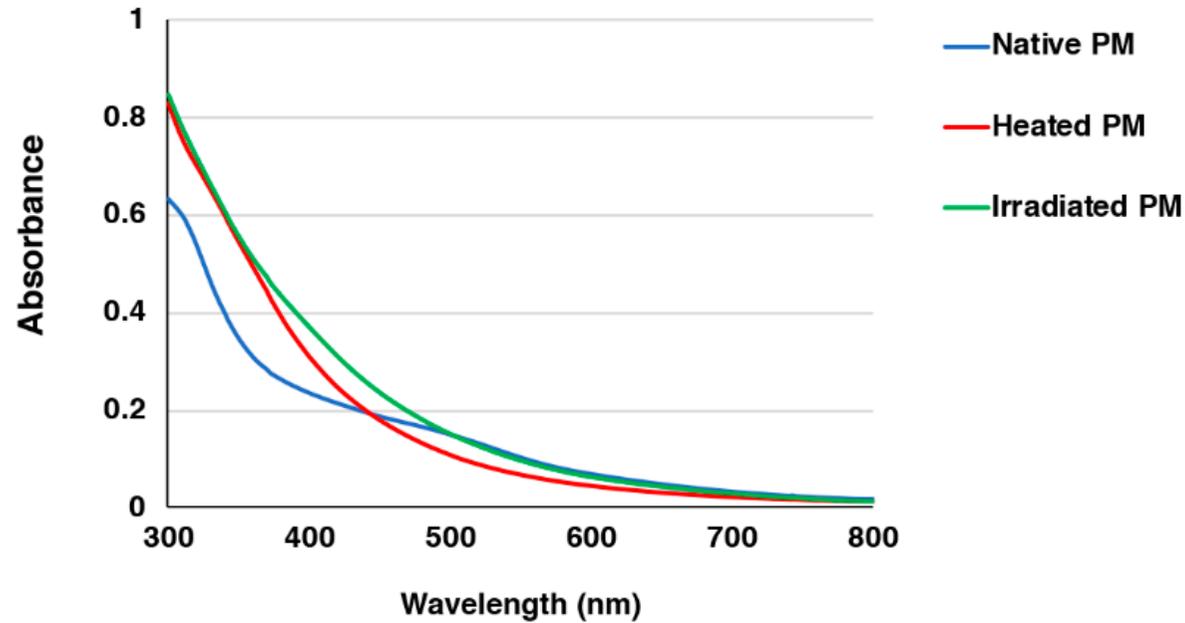
### **The Pro-oxidant Activity of Pheomelanin is Significantly Enhanced by UVA Irradiation: Benzothiazole Moieties are More Reactive than Benzothiazine Moieties**

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Figure S1



UV-VIS absorption spectra of native PM, heated PM and irradiated PM. Spectra were measured on solutions at a concentration of 40  $\mu\text{g/ml}$  of 0.05 M sodium phosphate buffer, pH 6.8. Spectrophotometric analysis revealed some difference between the three synthetic pheomelanins; native PM had an absorption with a shoulder around 500 nm, but heated PM and irradiated PM had not these shoulders. The irradiated PM and the heated PM showed an increase in integrated absorbance (320-400nm) of 48% and 56% compared to the native PM.

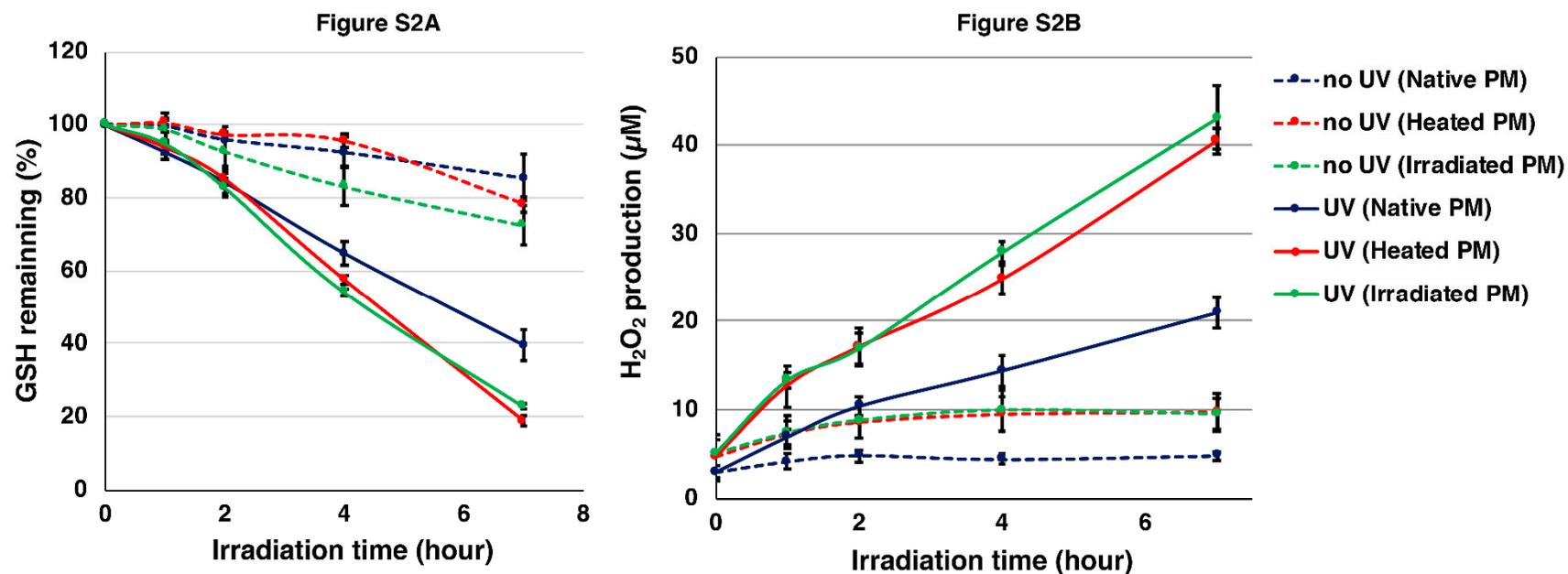


Figure S2A shows the time course of GSH remaining in suspensions of synthetic PMs exposed to UVA. GSH levels in heated PM, UVA-irradiated PM and native PM decreased rapidly after UVA irradiation. After 7 hours of UVA irradiation, 81% and 70% of GSH were depleted in heated PM, UVA-irradiated PM and native PM, respectively. On the other hand, GSH depletion decreased slowly in the case of no UV irradiation. Figure S2B shows the time course of H<sub>2</sub>O<sub>2</sub> production in suspensions of synthetic PMs exposed to UVA. H<sub>2</sub>O<sub>2</sub> production after 7 hours of UVA irradiation in heated PM, UVA-irradiated PM and native PM increased after UVA irradiation. H<sub>2</sub>O<sub>2</sub> production in heated PM and UVA-irradiated PM increased two-fold compared to native PM after UVA irradiation. On the other hand, H<sub>2</sub>O<sub>2</sub> production did not increase in the case of no UV irradiation. Data reported are means  $\pm$  SEM of three experiments.

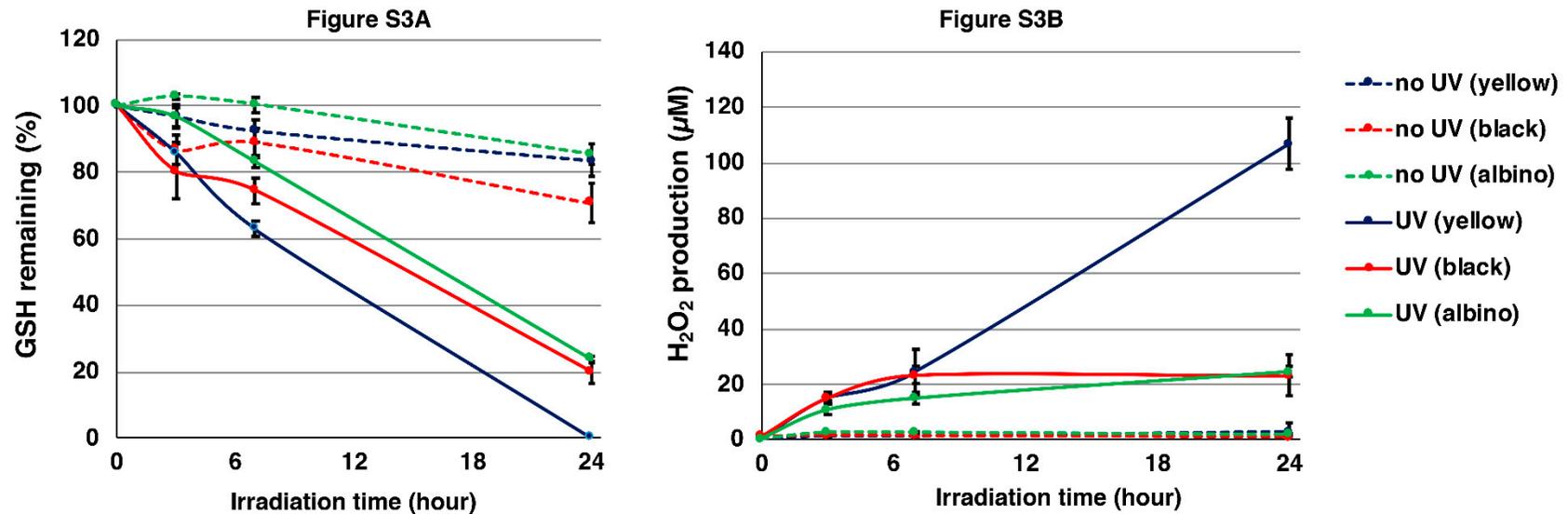


Figure S3A shows the time course of GSH remaining in suspensions of mouse hairs exposed to UVA. GSH in yellow, black and albino mouse hairs decreased rapidly after UVA irradiation. After 24 hours of UVA irradiation, 80% and 75% of GSH were depleted in black and albino hairs, respectively, but GSH was completely depleted in yellow hairs after 24 hours of irradiation. On the other hand, GSH depletion decreased slowly in the case of no UV irradiation. S3B shows the time course of H<sub>2</sub>O<sub>2</sub> production in suspensions of mouse hairs exposed to UVA. H<sub>2</sub>O<sub>2</sub> in yellow mouse hairs after 24 hours of UVA irradiation was produced at a high level (107 μM) after UVA irradiation, while it was at the trace level in black (23 μM), and albino mouse hairs (25 μM), respectively. On the other hand, H<sub>2</sub>O<sub>2</sub> did not increase in the case of no UV irradiation. Data reported are means ± SEM of three experiments.

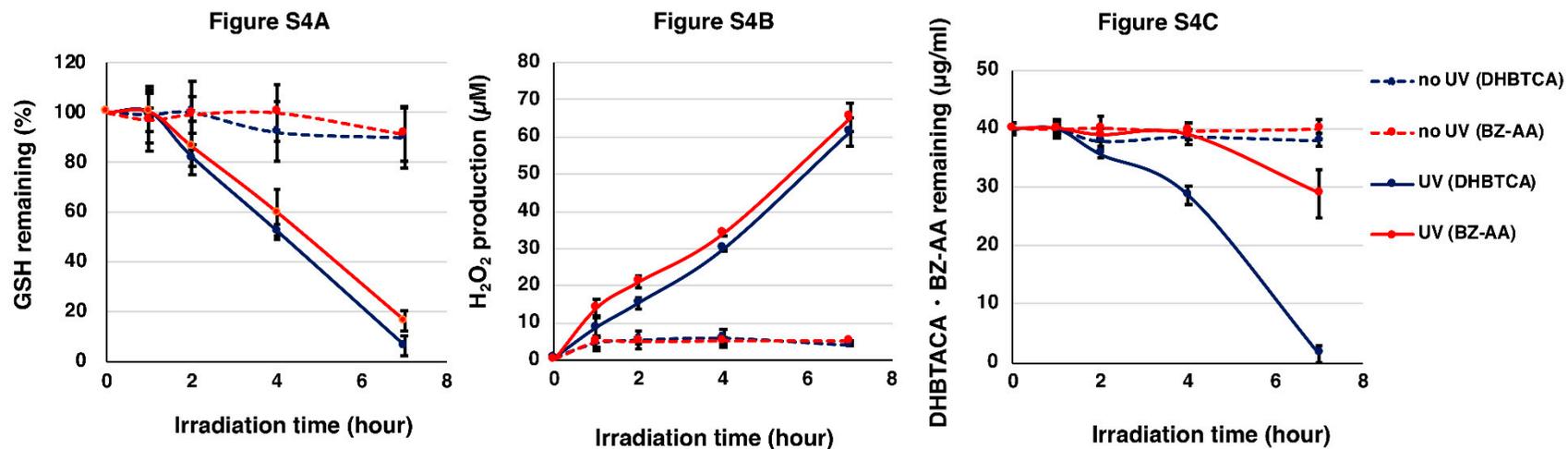


Figure S4A shows the time course of GSH remaining in suspensions of mouse hairs exposed to UVA. GSH in DHB-TCA and in BZ-AA decreased rapidly after UVA irradiation. After 7 hours of UVA irradiation, 6% and 17% GSH were remaining in DHB-TCA and BZ-AA, respectively. On the other hand, GSH depletion decreased slowly in the case of no UV irradiation. Figure S4B shows the time course of H<sub>2</sub>O<sub>2</sub> production in suspensions of DHB-TCA or BZ-AA exposed to UVA. H<sub>2</sub>O<sub>2</sub> production after 7 hours of UVA irradiation of DHB-TCA and BZ-AA increased after UVA irradiation. On the other hand, H<sub>2</sub>O<sub>2</sub> production did not increase in the case of no UV irradiation. Figure S4C shows the time course of the remaining DHB-TCA and BZ-AA during UVA irradiation. DHB-TCA decreased rapidly after UVA irradiation. On the other hand, BZ-AA decreased gradually. After 7 hours of UVA irradiation, the remaining DHB-TCA and BZ-AA decreased

by up to 2  $\mu\text{g/ml}$  and 29  $\mu\text{g/ml}$ , respectively. However, they did not decrease significantly in the absence of UVA irradiation. Data reported are means  $\pm$  SEM of three experiments.