

Analysis of human skin tissue after exposure to ionizing radiation enabled by GC-MS-based metabolomics

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Overview

- GC-MS based global metabolomics analyses were performed on human skin tissue exposed to different dosages (3, 10 or 200 cGy) of ionizing radiation and cultured for 3, 24, or 48 h post-irradiation.
- The levels of some metabolites were significantly perturbed after low dose radiation.
- Quantitative and qualitative differences in metabolites were dependent on both the irradiation dosages and time post-irradiation.
- These metabolites may be potential dosimetry markers for exposure to low dose ionizing radiation.

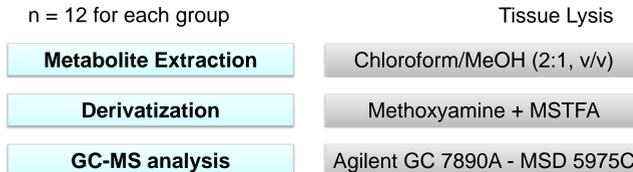
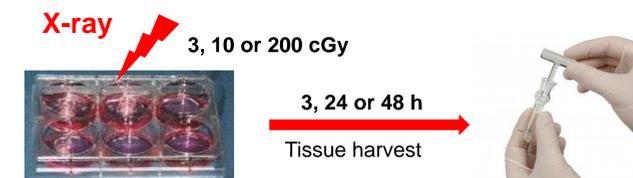
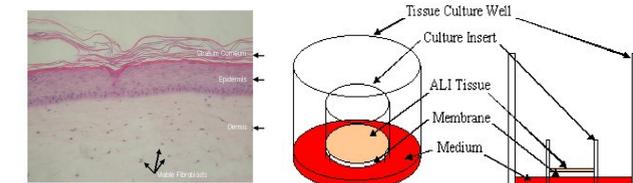
Introduction

- Exposure to ionizing radiation due to radiological accidents, medical imaging procedures, or terrorism is a major public health concern.
- Understanding the biological responses at a systems biology level and identifying biomarkers of ionizing radiation are important;
- Previous studies¹⁻³ reported changes in metabolite abundance after exposures to HIGH doses ionizing radiation in various samples;
- No study has yet been reported on the effects of LOW dose radiation exposure on the metabolome.
- We performed GC-MS-based metabolomics analyses to examine the metabolic perturbations in a human skin tissue model after exposure to different doses (3, 10 or 200 cGy) of ionizing radiation at different time points (3, 24 or 48 h) post-irradiation.

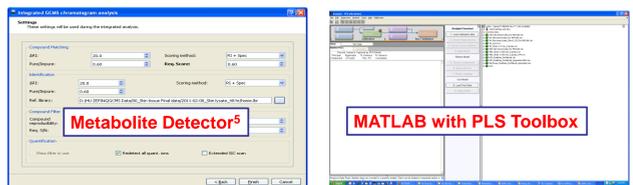
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Methods

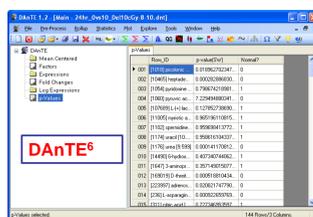
Sample preparation⁴ and analysis



Data analysis



Deconvolution, Integration and Identification



Wilcoxon rank sum test with Bonferroni correction

PCA and PLS-DA

To help reduce the possibility of type I errors, the critical p -value was modified using a Bonferroni correction, which was calculated by dividing 0.05 with the number of parallel comparisons.

Results

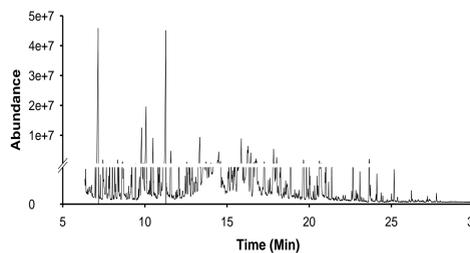


Figure 1. Representative GC-MS chromatogram of metabolites extracted from cultured human skin tissue.

Table 1. The numbers of features that showed statistical significance between the irradiated and mock-irradiated tissues at different time points

Time post-irradiation	3 cGy vs mock	10 cGy vs mock	200 cGy vs mock
3 h	0	0	6
24 h	0	1	14
48 h	22	42	29

Wilcoxon on Rank-Sum Test with Bonferroni correction and unequal variances assumed ($p < 0.05$).

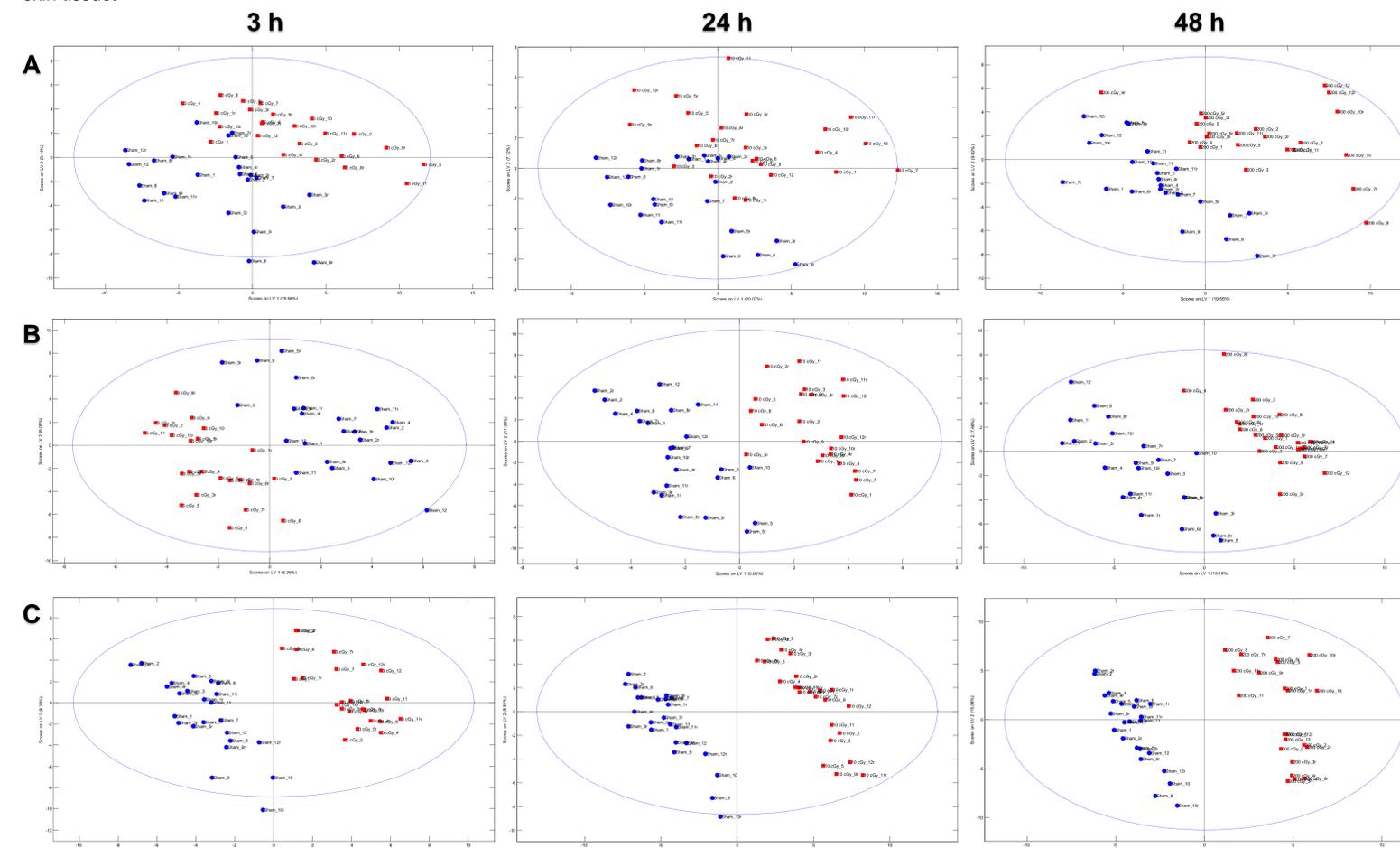


Figure 2. PLS-DA scores plots of GC-MS variables detected from human skin tissue separating different radiation dosages (3, 10 or 200 cGy) at different time points (3, 24 or 48 h) post-irradiation. **A:** 3 cGy vs mock; **B:** 10 cGy vs mock; **C:** 200 cGy vs mock.

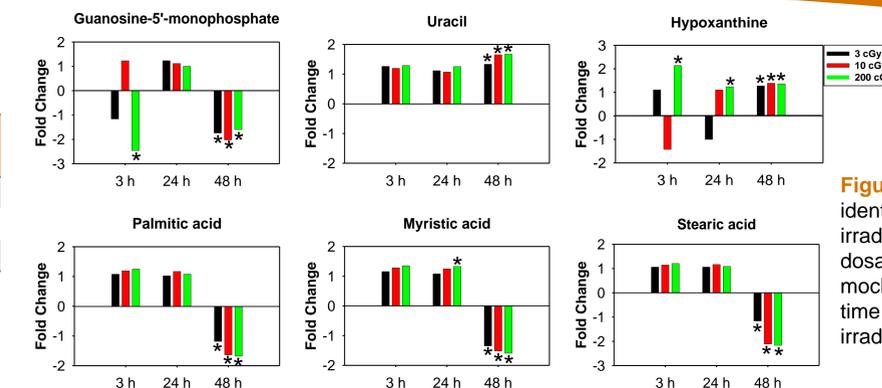


Figure 3. Significant metabolites identified from comparisons of irradiated tissue at different dosages (3, 10 or 200 cGy) with mock-irradiated tissue at different time points (3, 24 or 48 h) post-irradiation. *, $p < 0.05$.

Conclusions

- GC-MS-based metabolomics platform was successfully utilized to identify perturbations in the metabolome of human skin tissue exposed to low dose radiation.
- Metabolites displaying significant up- or down-regulation include those involved in the nucleotide metabolism, fatty acid metabolism, and glycolysis.
- The biological responses induced by low dose radiation, as indicated by the metabolic perturbations, were dose- and time-dependent.
- These significantly perturbed metabolites are worth further study as potential biodosimeters of low dose radiation exposures.

Acknowledgements

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