Metabolomic understanding of cell apoptosis derived by caffeine in HepG2 cancer cells

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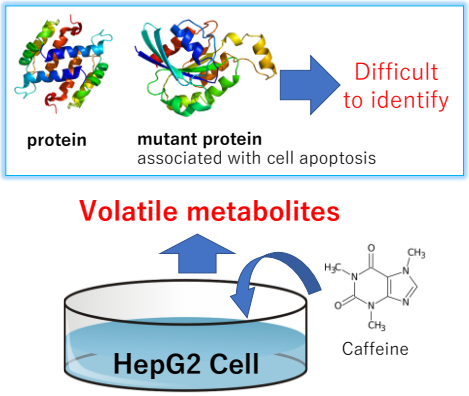
Normally, abnormal cells such as cancerous cells, senescent cells, and virus-infected cells in our body are killed by apoptosis. Apoptosis is programmed cell death, and its antonym is called necrosis.[1] While an elaborate molecular mechanism controls apoptosis, necrosis can be defined as accidental cell death without a molecular mechanism triggered when cells are physically or chemically damaged. Caffeine was isolated by German chemist Runge in 1820, and its molecular structure was known in 1897. Due to central nervous system stimulation, excessive caffeine intake causes dizziness, increased heart rate, anxiety, excitement, tremors, insomnia, nausea, and diarrhea. In this study, we examined the influence of caffeine on cell apoptosis, which resulted in the production of volatile metabolites that reflect cell activity.

(a)



(b)

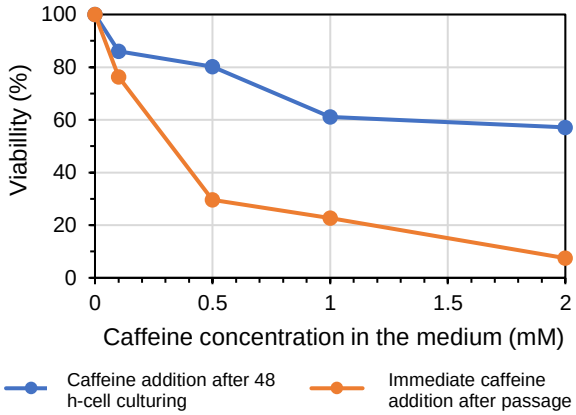


Figure 1. (a) Concept of this study and (b) tracking of cell viability according to timing of caffeine addition to HepG2 cells.

Figure 1a shows the concept of this study, investigating the presence of volatile metabolites generated by adding caffeine to HepG2 cells. Caffeine was introduced immediately after passaging, and cell counting was performed after four days of culture. This approach introduced caffeine before the cells adhered to the dish. Namely, this result means cell death due to the inhibition of cell adhesion also can be observed. To avoid this problem, caffeine was introduced two days after cell passaging. Cell counting was performed after four days of culture to compare differences in the number of cells surviving. Figure 1b shows that the number of cells surviving tends to decrease as the caffeine concentration increases. Indeed, it can be seen that the survival rate of cells is low when caffeine is added immediately after passage. When caffeine is added immediately after passaging, cell viability rapidly decreases and is reduced to approximately 10% of the normal passaging without caffeine. However, when caffeine was introduced after 48 h-cell culturing, cell viability increased to about 60%, even at a concentration of 2 mM. These results imply that cell adhesion is important when investigating caffeine-induced cell apoptosis. We will also report details of volatile metabolites associated with caffeine-induced cell death in a presentation on the day.

References

[1] S. Elmore. Apoptosis: A Review of Programmed Cell Death. Toxicol. Pathol. 2007, 35(4), 495–516. https://10.1080/01926230701320337.