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HTT35-04 Room:311 Time:May 1 09:45-10:00

## Development of C14-free laboratory animals.

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In the early stage of pharmaceutical researches,  $^{14}$ C labeled chemicals with very high radioactivity are administrated to laboratory animals to study pharmacokinetics. However, when  $^{14}$ C/ $^{12}$ C of the laboratory animals could be reduced, the radioactivity level of the chemicals is expected to be reduced lower. Also when  $^{14}$ C-free (DC; denoted as dead carbon) laboratory animals were developed, the radioactivity level for the study is expected to be reduced down by five orders of magnitude or lower by using AMS technique. That means that we need not the  $^{14}$ C labeled chemicals but natural level chemicals for the study of pharmacokinetics. In this case, it is also expected that we can be free from the hazardous high radioactivity and from the strictly regulated troublesome laboratory to handle the high level radioactive materials.

In Dec. 2010, we started the project to produce <sup>14</sup>C-free lives as feed for the <sup>14</sup>C-free laboratory animals. This is a preliminary report on the project, and parts of the investigation were already reported at 13th Japanese Symposium on AMS (Kobayashi et al., 2011). Here will be also introduced some recent studies.

When lives were cultivated in DC surroundings they grow up inevitably to be DC lives. For example, photosynthetic lives like vegetables or some kinds of microbes with chloroplast like euglena (midorimushi; in Japanese) can easily be DC lives when they were cultivated in DC surroundings.

For the first step, we cultivated some plants and euglena using  $^{14}$ C free water set in a glove box that was filled with artificial air (N<sub>2</sub>, O<sub>2</sub> and dead carbon CO<sub>2</sub> with proper concentration) irradiating with some artificial lights.  $^{14}$ C concentrations in the plants and the microbes were measured by AMS. Since the modern carbon (natural carbon) CO<sub>2</sub> could not be perfectly removed from the air and the water and air tightness of the glove box system was also not perfect, the percentages of dead carbon to modern carbon (DC ratio) in the samples could not be higher than about 80 %.(Kobayashi et al., 2011a; Kobayashi et al., 2011b)

While investigating the cause of the imperfect DC ratio, we got 96% DC Euglena by using a little different way. That is to use a small glass bowl with an airtight lid, in which were set  $CO_2$  tablets, a small amount of chemical fertilizer and Euglena. From outside of the bowl, fluorescent lamps irradiated adequate amount of light to them. One or two months later, the euglena was carefully collected on glass filters in a glove box filled with DC air.  $^{14}C/^{12}C$  of the euglena was measured by AMS and the  $^{14}C$  concentration was  $3.71\pm0.02$  pMC (percent Modern Carbon) which leads to DC ratio as 96% (Kobayashi et.al., 2012).

In order to make sure that mice really eat the euglena tablets, we fed the mice with euglena tablets which were mixed with chlorella powder by 20%. The tablet is on the market for people as a health food. After three months feeding on three mice, there were no large differences compared to the other three mice which were fed by ordinary food for comparison. The experiment concluded that mice will grow up healthy by eating the euglena tablet.

Those two above data show the possibility to realize the DC animals.

Recently, we have started to extend the project to realize for business, supported by a grant.

## References:

Kobayashi, K. et al. (2011a), Production of <sup>14</sup>C-free plants and animals (in Japanese); Kobayashi, K. et al. (2011b), Production of <sup>14</sup>C-free plants and animals; Kobayashi, K. et al. (2012), Production of dead carbon lives (in Japanese)

Keywords: Pharmacokinetics by AMS, C14-free lives, Euglena

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