Effect of probenecid on 3D-cultured prostate cancer spheroids

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Probenecid is a well-known uricosuric agent used for gout treatment through blockage of urate transporter in renal tubules. On the other hand, probenecid can also inhibit multiple channels and transporters including multidrug resistance protein-1 (MRP-1). Therefore, probenecid might support the effect of anti-cancer drugs via inhibition of efflux of these drugs from tumor cells.

Conventionally, cancer cell lines have been cultured as two-dimensional (2D) monolayer. However, such condition does not reflect the real tumor situation in vivo. Recently, 3D culture techniques have developed to examine the cancer cell lines with more natural tumor property. In this study, we evaluated the effect of probenecid on prostate cancer cell lines which cultured as multicellular tumor spheroids by culturing in ultra-low attachment plate.

Prostate cancer cell line 22Rv1 cultured as spheroid showed lower sensitivity against anti-cancer drug doxorubicin, compared to cells cultured as monolayer. Probenecid treated-spheroid was more sensitive against doxorubicin. Interestingly, we found that probenecid itself has anti-tumor activity in concentration dependent manner. Probenecid was more effective to 3D cultured spheroid than 2D cultured monolayer. In this presentation, we also show the result of other prostate cancer cell lines and discuss the anti-cancer mechanism of probenecid.