Development of a curcumin monoglucuronide as an anticancer prodrug targeting KRAS-NF-κB pathway

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Summary
- KRAS-NF-κB signaling pathway plays a pivotal role in tumor progression
- Preclinical cancer models have shown that curcumin, a natural polyphenol, can suppress tumor growth through NF-κB pathway.
- We have succeeded in developing an injectable form of curcumin (curcumin monoglucuronide: CMG), which could achieve more than 1,000-fold higher plasma curcumin levels compared to those with orally administered curcumin.
- CMG showed anticancer effects in xenograft mouse model.
- We are now moving forward to develop CMG as a novel anticancer drug.

Introduction
- KRAS-NF-κB signaling pathway plays a pivotal role in tumor progression 1-3).
- Preclinical cancer models have shown that curcumin can suppress tumor growth through NF-κB pathway 4-6).
- However, curcumin is highly hydrophobic and orally administered curcumin is poorly absorbed into the human body, and its clinical application has been hampered 7, 8).

Aim
To overcome the poor bioavailability of curcumin, we have developed an injectable form of curcumin (hydrophilic curcumin monoglucuronide: CMG) and tested its pharmacokinetics and anticancer effects in preclinical models.

Results
- Intravenous administration of synthetic CMG is transformed into active curcumin at levels more than 1,000-fold higher than those with orally administered curcumin in the rat model 9).

Results (continued)
- CMG showed anticancer activity in xenograft mouse model of human colon cancer (HCT116).

Conclusions
- We succeeded in overcoming the problem of poor bioavailability of curcumin by developing an injectable CMG (patent pending).
- We are now moving forward to develop CMG as a novel anticancer drug with collaboration with TheraBioPharma Inc.

Possible mechanisms of anticancer effects of CMG

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