Efficacy and toxicity of extract of sprout-forcing grape seeds for anti-pancreatic cancer by new 1h phenotypic screening

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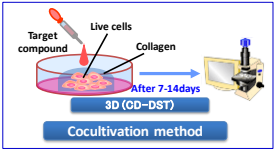
Summary

We successfully developed a rapid phenotypic screening method (HP-SPR-3D) for reliable prediction of efficacy and toxicity for anti-cancer drugs. This enables the evaluation at physiological conc. within 1h after the drug addition regardless to the pharmaceutical mode of action and indirectly relates to clinical test. We applied HP-SPR-3D to evaluate extract of sprout-forcing grape for anti-pancreatic cancer. The extract of sprout-forcing grape seeds by water (iGS4000) was supplied by Japan Biomedicine Co., Ltd. It was further treated by digestion and absorption model test using digestion enzymes and others to prepare valid compounds in case of its oral administration and used. Human pancreatic cancer cell Mia PaCa-2 was used. The 2D cultured cells were self-attached to an HP-SPR-3D sensor chip and covered by collagen to activate cells into in vivo-like cell status, and monitored for 1h with prepared samples. The extract of sprout-forcing grape seeds showed excellent anti-pancreatic cancer efficacy even compared to doxorubicin and paclitaxel.

Conventional technology -Cell-based assay-

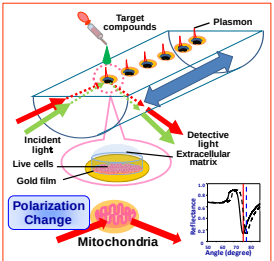
Rapid and reliable *in vivo*-like test is demanded



Disadvantage

- Complicated handling
- Medium exchange
- Long decision duration
- Label requirement
- Large test error
- Many cells（10^6）
- Difficulty in evaluation of toxicity properties

Emerging technology −HP-SPR-3D method−



Breakthrough
Custom-made instrument with 10K to 1M times higher sensitivity compared to commercial one.

Breakthrough
Early mitochondrial polarization change rate after compound addition is a key to quantitatively predict the final efficacy and toxicity properties!

Breakthrough
3D cell activity is obtained by conditioning of 2D attached cells covered by extra cellular matrix for short time with no cell division !

Within 1 hour

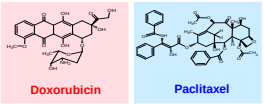
HP-SPR-3D method

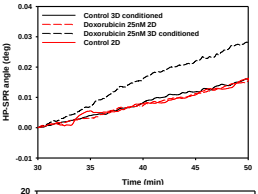
Advantage

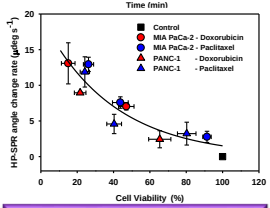
- Easy handling
- Medium exchange free
- Rapid decision duration
- Label free
- Small test error
- Limited cells（1000）
- High reliability in polypharmacy
- Compatibility with conventional results
- Physiological concentration evaluation
- Simultaneous evaluation of efficacy and toxicity properties

HP-SPR-3D vs CD-DST

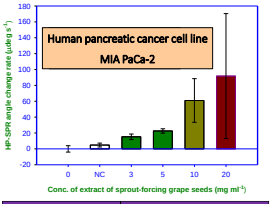
Anti-cancer drugs







Sprout-forcing grape seeds



Conc. of extract of sprout-forcing grape seeds (mg ml⁻¹)	Efficacy
0.0	Control
Negative control (NC)	Negative control (No difference to Control)
0.1	No difference to Control
1.0	No difference to Control
3.0	Anti-cancer (Apoptosis)
5.0	Anti-cancer (Apoptosis)
10.0	Anti-cancer + Toxicity (Necrosis)
20.0	Toxicity (Necrosis)

COI Disclosure Information

Toshihiro ONA

I have the following financial relationships to disclose.

Leadership position/advisory role for: **O'Atari Inc.**
Stockholder in: **O'Atari Inc.**
Patents and royalties from: **Kyushu Univ.**
Honoraria(lecture fee) from: **None**
Honoraria(manuscript fee) from: **None**
Grant/Research funding from: **Physical Co., Ltd.**
Other remuneration from: **O'Atari Inc.**