Supplementary Information

Active learning framework with iterative clustering for bioimage classification

Natsumaro Kutsuna, Takumi Higaki, Sachihiro Matsunaga, Tomoshi Otsuki,
Masayuki Yamaguchi, Hirofumi Fujii & Seiichiro Hasezawa

Supplementary Methods
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MRI imaging of cancer cells

All animal experiments were conducted according to the protocols approved by the institutional animal experimental committee. Eleven male ddY mice (4 weeks old) and 8 female CH3/He mice (4 weeks old) were purchased from Japan SLC, Inc (Hamamatsu, Japan). They were housed 4–5 per cage under the controlled lighting conditions of a 12-hour light and 12-hour dark cycle. The room temperature and humidity were kept at 22 ± 2 °C and 50%, respectively. After 2–5 weeks of acclimatization, $1 \times 10^6$ Sarcoma 180 cells and $5 \times 10^6$ FM3A cells, which were maintained in our laboratory, were inoculated in the thigh of ddY and CH3/He mice, respectively. After 15–28 days of inoculation, the mice underwent imaging by an MRI scanner and scan protocols are described below. During the MRI examination, mice were anesthetized with 1–2% isoflurane and a gas mixture of N2O and O2 administered via a nose mask.

All MR images were obtained using a 3 Tesla whole body MRI scanner (Signa HDx; GE Healthcare, Wisconsin, United States). Either a transmit-receive radiofrequency (RF) coil (birdcage type, 5 cm in inner diameter [ID], 11 cm in length) or a receive-only
coil (solenoid type, 3.5 cm ID, 6 cm in length) was used. For the receive-only coil, RF transmission was performed using a body coil combined with a whole body MRI scanner. These coils permit homogeneous signal sensitivity when measuring mouse tumors. After anesthesia was introduced, the mouse was placed in the prone position with its tumor located near the center of the coil to obtain the best possible MR signals from the tumor. In all mice, T2-weighted images were obtained using a two dimensional fast-spin-echo sequence with a repetition time of 3,500–4,000 ms, a nominal effective echo time of 60 ms, and echo train length of 8. Six to 12 cm field-of-views (FOVs) with a 256 × 160–256 matrix (zero-interpolation [ZIP] to 512 × 512) yielded an in-plane resolution of 117–234 × 117–234 μm for coronal images. Transverse images were obtained with a resolution of 78 × 78 μm and a FOV of 4 cm and 256 × 160 matrix (ZIP to 512 × 512). The slice thickness and slice gap were 1 mm and 0–1 mm, respectively. Eleven to 15 coronal slices and 11–30 transverse slices around tumors in the thigh were obtained within 2’ to 3’ 30”, and 3’ 30” to 4’ 26”, respectively, with a number of excitations of 2. After MR image acquisitions, data were transferred to a workstation (Advanced Workstation version 4.3; GE Healthcare, Wisconsin, United States) via a closed network. All image data with digital imaging and communication in medicine (DICOM) format were recorded on compact disc read-only memories (CD-ROMs) and
Imaging and analysis of stomata

To capture images of stomata in *Arabidopsis thaliana*, the abaxial leaf epidermis was peeled off and floated, with its inner surface facing down, on a glass slide with basal buffer (50 mM KCl, 5 mM MES-Tris (pH 6.5) and 10 mM CaCl$_2$) and was finally covered by a coverglass (Matsunami, Osaka, Japan). The glass slide was placed onto the inverted platform of a microscope (IX70, Olympus, Tokyo, Japan) and image capture was performed with a cooled charged couple detector camera head system (CoolSNAP HQ, Photometrics, Tucson, Arizona, USA). To classify the stomata images, we developed new features based on the statistics of intensity on concentric circle (SICC) that are defined as 

$$\text{SICC} = (m_1, v_1, m_2, v_2, ..., m_R, v_R)$$

$$m_r = \frac{\sum_{\theta=0}^{2\pi} p(r, \theta)}{2\pi r} \quad \text{(S1)}$$

$$v_r = \frac{\sum_{\theta=0}^{2\pi} (p(r, \theta) - m_r)^2}{2\pi r} \quad \text{(S2)}$$
where $p(r, \theta)$ is intensity in the pixel located at $(r, \theta)$ from central pixel of image in polarized coordinate and $R$ is the maximum radius of the images. The value of $R$ is fixed at the half-length of the stomatal pore, 65 pixels.