Glioblastoma multiforme

* Most aggressive and fatal brain tumor
  * Ranks third in cancer death in young adults
  * Of the 10 to 15% of patients that can undergo surgery, recurrence occurs in 80% of the cases
  * Chemotherapy and Radiation therapy lead to poor efficacy
  * Therapies fail mostly because residual tumor cells become resistant to treatments

Alternative therapies such as Photodynamic Therapy (PDT), and knowledge on the pathogenesis of Gliomas could lead to improved treatment and prognosis.
Glioblastoma multiforme: multicell spheroid model

Human Brain Tumor

Sutherland, R.M.,
Science,

Human Brain Tumor in the Petri dish

A generous gift of G. Granger
UC Irvine

Collaboration with Dr. Henry Hirschberg and
Dr. Chung-ho Sun
Beckman Laser Institute
UC Irvine
Focus: live migrating cells

(a) Migrate in clusters

(b) Clearly interact with one another

(c) Majority is double-nucleated
Uptake of mitochondrial dyes identifies the mitochondria in ACBT glioblastoma model

MitoTracker Orange

- Nonfluorescent
- Fluorescent-cationic
- Fluorescent-conjugate

Uptake takes a few hours

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- Bubble formation
- Swelling
- Leaking Membranes

'Leaky Cells'

+ a mitochondrial dye

no dyes

Healthy Cells

'Leaky' Cells

Redox Index (NADH/FAD)

Graph showing comparison of Redox Index (NADH/FAD) between Healthy Cells and 'Leaky' Cells.
Fluorescence Intensity (arb. units)

Wavelength (nm)

535 nm

580 nm

F-actin

live mitochondria

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F-actin in the live migrating cells

7 days of migration

3 days of migration

• variety of F-actin filaments are observed

• migratory section of the cell is characterized by stress fibers and lamellipodium (lam)

• non-migratory section of the cell is composed of microspikes and filopodium (ms/fil) and is more circular
F-actin in the live migrating cells: Up and close

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