Mushroom Life Cycle

History of Medicinal Mushrooms

- Hot water decoctions from certain fungi long recognized to have health promoting effects, particularly in Eastern cultures
- ~300 species felt to have therapeutic potential, important in Asian cuisine and as folk medicines
- Crossover to West stimulated by:
  - Cancer epidemiology of *Flammulina velutipes* (enokitake) farmers
  - Isolation of specific active constituents
  - Superior organoleptic properties to dominant *Agaricus*
  - Multimillion $ US market for edibles and medicinals
Medicinal Mushrooms Constituents

- β-D-glucan backbone of active constituent
  - Linked to protein forms proteoglycan
  - Proteoglycans have greater immunopotentation activity
  - Sterols, phenols, terpenoids, fatty acids proteins, vitamins, minerals and trace elements also present

- Immune effects via stimulation of cytotoxic T cells and NK cell activity

Mechanism of Immune Action

- β-glucans resemble molecules on bacterial cell walls
- β-glucans complex with complement on macrophages, mobilizing immune response
- When ingested into macrophages, β-glucans stimulate cytokines active in tumor inhibition, i.e. IFN-γ, TNF-α, IL-2 and IL-12
- Differently branched glucans from different species stimulate T cells, NK cells or others
Anti-Cancer Activities

• Most mushrooms work as non-specific immuno-stimulants, enhance host response
• Activity may require intact T cell function
• Activity especially beneficial when used in conjunction with chemotherapy
• Some may have direct cytotoxic effects
• Most clinical trials and licensed drugs are in Asia; more studies needed

Trials of Mushrooms in Cancer: Issues in Design and Interpretation

• Information derived from:
  – In vitro effects
  – Animal models
  – Human trials
  – Epidemiologic observations
• Mushroom products studied:
  – Whole mushrooms: eaten, encapsulated or extracted
  – Mycelia or fruiting bodies
  – Extracts
    • Water: hot or cold
    • Ethanol
    • Isolated fractions

Trametes versicolor

• AKA Coriolus, Polyporus
• Turkey tail mushroom
• Yun Zhi (Cloud fungus)
• 2 proteoglycans
  – PSK (Krestin)
  – PSP
• Widely used adjuvant Rx in Japan and China
  – 25% of cancer care cost in Japan
  – Positive RCTs in GI (esp stomach) and breast
### Lentinus edodes

- Shiitake
- Xiang gu (Fragrant mushroom)
- LEM
  - Lentinus edodes mycelium
- Lentinan
  - Cell wall constituent extracted from fruiting bodies or mycelium
  - Widely used as adjuvant immunotherapy in Japan
  - High MW precludes oral administration
- Active Hexose Correlated Compound base

### Grifola frondosa

- Maitake
- Hen of the woods
- D-fraction
  - Found in mycelia and fb
  - Standardized β-1,3 and β-1,6 glucan fraction
  - MD-fraction is a more purified extract
  - Adaptogen and immunomodulator
  - May ↓ chemo side effects

### Ganoderma lucidum

- Reishi
  - 10,000 year mushroom
- Ling Zhi
  - Mushroom of immortality
- Polysaccharides immune enhancing activity
- Ganoderic acid triterpenoids inhibit tumor cell growth
- Worldwide extract sales 1.5 billion annually
Cordyceps sinensis

- Used for vigor and stamina
- Lung and kidney tonic
- Restores immune activity with chemoRx
- Prolonged survival of mice receiving chemoRx
- May also improve anemia from chemoRx

Hericium species

- May stimulate brain derived nerve growth factor
  - Could be considered as a neuroprotective agent vs chemo-induced neuropathy
  - Possible use in chemo-induced cognitive impairment
  - Human studies needed!

Agaricus species

- *Agaricus blazei* most common CAM Rx in Japanese cancer patients
- *Agaricus bisporus* may have aromatase inhibitor activity
  - Significance of agaritine in raw button mushrooms unclear
  - ALL mushrooms must be cooked before eating !!!
Mushrooms and Green Tea

- Case control study in SE China 2004-2005
- 1009 women with confirmed breast CA and 1009 age-matched controls
  - Compared with non-consumers
    - OR- 0.36 (95% CI 0.25, 0.51) for daily intake >10g fresh mushrooms
    - OR- 0.53 (95% CI 0.38, 0.73) for daily intake > 4 g dried mushrooms
    - ORs 0.11 and 0.18 for fresh and dried in combo with >1.05 g dried green tea leaf beverages/day
  - Effects seen in pre and post-menopausal women

Zhang et al, Int J CA, 2009

Medicinal Mushrooms and Cancer

- Useful properties against cancer
  - Anti-neoplastic
  - Antioxidant
  - Immunomodulatory
  - Anti-inflammatory
  - Aromatse inhibition
  - Antiviral
- Symptom management potential

Unanswered Questions

- Which mushroom(s) to use for which cancer patient?
- When to prescribe in relation to chemoRx?
  - Chemo interaction doubtful though feared
- How long should/can they be taken?
  - TCM may suggest seasonal adjustments
  - Long-term safety and efficacy unclear
- Are they safe in immune-related cancers?
MUSHROOMS AND CANCER
USEFUL REFERENCES
Donald I. Abrams, MD


Wu JY, Zhang QX, Leung PH. Inhibitory effects of ethyl acetate extract of *Cordyceps sinensis* mycelium on various cancer cells in culture and B16 melanoma in C57BL/6 mice. Phytomedicine 2007; 14:43-49.