Internet Appendix A37: Organic Chemistry

A37.1 Illustrative Pitch Template Example on Natural Products Synthesis

This pitch is reverse engineered from the paper:
Beekman, A. M., & Barrow, R. A. (2014). Syntheses of the fungal metabolites boletopsins 7, 11, and 12 from the Papua New Guinea medicinal mushroom Boletopsis sp. The Journal of organic chemistry, 79(3), 1017-1024.

Pitcher's name	Marita Smith	For category	Natural Products Synthesis	Date completed	9/6/15
(A) Working Title	Synthesis of fungal metabolites from novel medicinal mushrooms				
(B) Basic Research Question	Can we isolate the medicinal compounds from traditional medicinal mushrooms and devise synthetic pathways for their production?				
(C) Key paper(s)	Takahashi, A., Kudo, R., Kusano, G., and Nozoe, S. (1992). 5-Lipoxygenase inhibitors isolated from the mushroom Boletopsis leucomelas (Pers.) Fayod. *Chemical and Pharmaceutical Bulletin*, *40*(12), 3194-3196. Blackwell, M. (2011). The Fungi: 1, 2, 3… 5.1 million species?. *American journal of botany*, *98*(3), 426-438. Wossa, S. W., Beekman, A. M., Ma, P., Kevo, O., and Barrow, R. A. (2013). Identification of Boletopsin 11 and 12, Antibiotics from the Traditionally Used Fungus Boletopsis sp. *Asian Journal of Organic Chemistry*, *2*(7), 565-567.				
(D) Motivation/Puzzle	Natural products are an important source of new drugs and treatments. Many fungal metabolites have strong anti-bacterial and immune-strengthening actions and have long been used in traditional medicine, particularly in Chinese and Ayurvedic cultures. Mushrooms are also a crucial part of medical practices in Papua New Guinea. The extraordinary biodiversity, harsh terrain and limited outside contact make Papua New Guinea one of the remaining frontiers in enthnomycology. Boletopsins are a class of compound that have been identified in Japan from the *Boletopsis* species of mushroom. These compounds have been shown to be active against human pathogenic bacteria. Preliminary studies of similar species used by the Kiovi tribe in Papua New Guinea indicate the production of unique Boletopsins. Further study of these compounds, their function and long-term synthesis potential would be beneficial and potentially provide new medical treatments.				
THREE	Three core aspects of any empirical research project i.e. the "iDioTs" guide				
(E) Idea?	Characterising the compounds used in mushrooms traditionally used by the Kiovi tribe of Papua New Guinea should provide a spectrum of new natural products potentially useful to humans. By characterising these compounds and assessing their treatment potential, targets can be identified for natural products synthesis. Once the activity of these compounds has been demonstrated, synthetic pathways to artificially produce these targets in a lab environment could be devised for further testing and potential pharmaceutical use.				
(F) Data?	-*Boletopsis* sp. mushrooms identified and picked with help of the Kiovi tribe and transported back to Australia -Compound extraction and identification -Analysis of compound activity				

(G) Tools?	-Kiovi guides and collection equipment -Suite of analytical tools, including mass spectrometer and nuclear magnetic resonance imager -Biological testing for activity against pathogens -Synthetic laboratory for extraction and compound synthesis
TWO	Two key questions
(H) What's New?	The *Boletopsis* sp. mushrooms, traditionally used to treat gastrointestinal complaints by the Kiovi tribe of Papua New Guinea, have never been fully characterized. The identification of new Boletopsin compounds may lead to the development of new natural products useful to human drug synthesis.
(I) So What?	New pharmaceutical targets are in demand. The identification of natural products can be slow and time consuming. Working with the traditional medicine knowledge of remote indigenous communities may fast-track the development of relevant drug compounds. Additionally, the identification of novel compounds broadens scientific knowledge of fungal metabolites and their function.
ONE	One bottom line
(J) Contribution	The primary source of the contribution will be the identification of a suite of novel fungal metabolites produced by *Boletopsis* sp. mushrooms from Papua New Guinea, in addition to their potential medicinal applications and routes of synthetic synthesis.
(K) Other considerations	Is Collaboration needed/desirable? -Idea: yes; -Data; yes – need to work closely with members of the Kiovi tribe -Tools; yes –representatives and funding from various institutions preferred Target journals – *Organic Chemistry, Journal of Natural Products* "Risk" assessment: -"no result" risk: low. Boletopsins have been identified in other *Boletopsis* sp. mushrooms in Japan, therefore it is likely that similar compounds will be present in the Papua New Guinea mushrooms. -"competitor risk"(i.e. being beaten by a competitor): low. Papua New Guinea is relatively inaccessible and a study of this scope will require a small team to work closely with traditional tribes for a long period of time. -risk of "obsolescence": Low. The demand for new drug targets is on the increase and fungal metabolites exhibit extraordinary potential.