



This research has allowed a systematic study of *Scutellaria* germplasm for evaluating anti-cancer properties of plant extracts and its flavonoid constituents. We have also carried out field studies to optimize various agronomic parameters to obtain higher biomass, flavonoid compounds, and number of harvests. Plant-based medicines have an annual market over USD 60 billion worldwide and most of the raw material is still wildcrafted. Many species will be suitable to grow as premium crop by farmers in the SE USA.

## GERMPLASM CONSERVATION, ANTI-ADIPOCYTIC AND ANTICANCER ACTIVITY, AND METABOLIC ENGINEERING IN THE GENUS SCUTELLARIA

### Who cares and why?

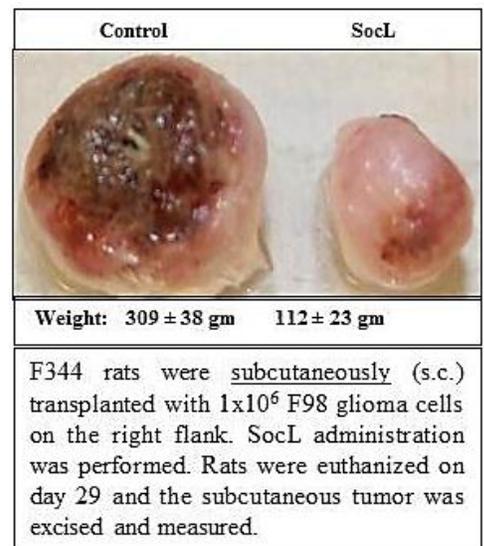
Plants of the genus *Scutellaria* (family Lamiaceae; mint family) are distributed globally and they are an integral part of Eastern as well as American traditional medicine. The genus *Scutellaria*, commonly referred to as skullcap, is considered as a North American perennial plant. At present this genus is represented by 350-360 species all over the Northern Hemisphere. Many species are rare, threatened, or endangered. Habitat destruction, urbanization, and poor seed set are a few reasons behind the diminishing population of many skullcaps. Importance of studying species that are endangered due to climate change and habitat destruction is urgent. The *Scutellaria* species has potential benefits that may improve human health and are thus worthy of research. More than 295 compounds have been isolated from the *Scutellaria* species and the majority of the compounds are flavonoids and diterpenes. We have developed a germplasm collection at Fort Valley State University (FVSU) that includes 21 species. These species are maintained in the greenhouse and through micropropagation in the lab. Biotechnology presents significant advances for the use of *Scutellaria*. We present progress in micropropagation, transformation for desired gene transfer and hairy root induction, extraction and HPLC analysis of targeted flavonoids, and pre-clinical and clinical studies on select extracts and isolated flavonoids using glioma tumor model.

### What has the project done so far?

Strong collaborations and partnerships have led to the team's success.

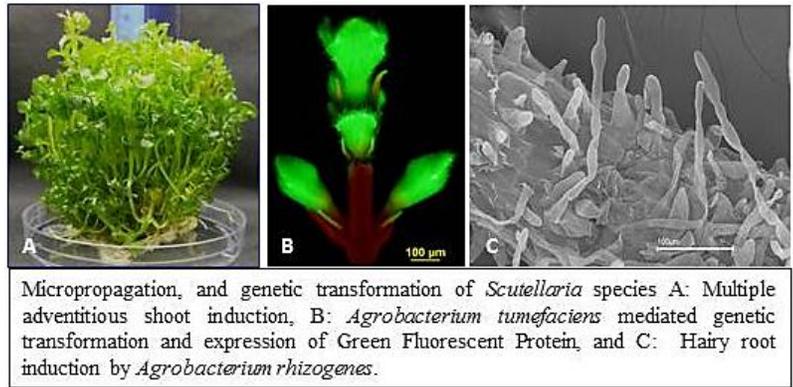
**Biomedical studies:** Potential anti-adipocytic and anticancer properties of *Scutellaria*: The applicability of *Scutellaria* extracts clinically rests on a pathway-based theory of cancer. By interrupting malfunctioning cellular signaling and metabolic mechanisms, cancer cell proliferation can be attenuated and thus clinical gains can be achieved. *Scutellaria* extracts were found to have potential anti-adipocytic and anticancer properties.

**Biomedical studies:** Potential anti-adipocytic and anticancer properties of *Scutellaria*: We have recorded anti-invasive potential of SocL extract and constituent flavonoids in an organotypic invasion assay (glioma invasion across 50 $\mu$ M brain slices) in vitro. We observed significant inhibition of glioma cells by SocL extract as well by flavonoids wogonin and luteolin. Western blot analysis also revealed inhibition of matrix metalloproteinase 2 (MMP2) following treatment of glioma cells with SocL extract and constituent flavonoids for 48 hours. Moreover, inhibition of MMP-2 activity was associated with a concomitant inhibition of TGF- $\beta$ 1 signaling activity, suggesting that the two processes could be inter-related.



**Hairy Root Culture and Metabolic Engineering:** Hairy Root Culture and Metabolic Engineering: Plants contain a MYB-protein subfamily that has been seen as key factors in controlling development, metabolism and responses to biotic and abiotic stresses. It has also been found that these proteins can regulate biosynthetic

pathways. In order to manipulate the levels of bioactive flavonoids in *Scutellaria lateriflora*, we expressed the *Atmyb12* flavonoid-specific transcription factor in hairy roots. Overall, all the transgenic hairy root lines expressing *Atmyb12* gene showed much higher levels of a wogonin-derivative. Ongoing research is focused to confirm the identity and yield of the putative wogonin derivative.



## Impact Statement

- **Conservation:** *Scutellaria* germplasm collection is being established for future research, material exchange with other researchers, and conservation. We have developed *in vitro* conservation protocols for 21 species including *S. ocmulgee* that is endemic to Georgia and *S. montana* which is federally endangered.
- **Field studies to develop agronomic practices:** This will help farmers to grow *Scutellaria* as a premium crop.
- **Metabolic engineering:** Transgenic protocols using *A. tumefaciens* and *A. rhizogenes* have been optimized to develop mechanisms to enhance therapeutic molecule production and assist pharmaceutical industry.
- **Biomedical research:** Our data suggest that extracts have specific anti-tumor (glioma cells) activity and in future can be used as an adjunct to other therapies.
- **Anti-adipocytic activity:** Our preliminary studies show that *Scutellaria* extracts are capable of blocking conversion of pre-adipocyte cells into adipocytes (fat cells) without cytotoxicity.
- **Biotechnology research/education:** This project fulfills the goal of sensitizing / training high school / graduate students in research areas like conservation/cryopreservation, transgenics, phytochemical screening, and cancer and obesity biology.

### What research is needed?

Many skullcap species have showy, beautiful blooms with great potential as ornamental plants. Rare and endangered species exhibit poor seed set and that is a serious concern. Pollination biology assisted by scanning electron microscopic studies have shown interesting differences in pollen output, anther dehiscence, and pollen germination and viability aspects. In hairy root studies, addition molecular analysis will be conducted to determine the mRNA levels of *Atmyb12* and other genes in the flavonoid pathway. All these lines are being investigated currently.

### Want to know more?

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