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Press Release

Sphinx molecule to rescue African farmers from witchweed

- Discovery of a hypersensitive suicide germination stimulant -

December 17, 2018

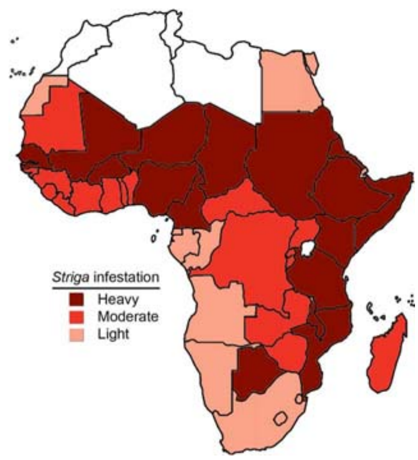
An interdisciplinary team led by researchers at Nagoya University has discovered a highly potent and selective molecule, SPL7, that can lead seeds of the noxious parasitic weed *Striga* to suicide germination. *Striga*, also known as witchweed, has seriously affected millions of hectares of crop fields in Africa and poses a major threat to food security. Nevertheless, an effective method to control *Striga* infestation remains a challenge. In a new study reported in *Science*, ITbM's chemists and biologists have come together to develop a promising molecule, SPL7, that selectively wither *Striga* at extremely low concentration. SPL7 is expected to alleviate *Striga* infestation and save crop losses worth of billions of U.S. dollars every year.

Nagoya, Japan – In various parts of sub-Saharan Africa, purple-pink flowers can be seen covering crop fields. While beautiful in sight, the plants with pink flowers parasitize through root system withdrawing minerals and water from crops and, thus, leading to the withering of the host before bearing grains. The plant, known as *Striga hermonthica* (*Striga*) or witchweed, is an African native parasitic plant which has co-evolved with sorghum as its natural host. Grown into 1 meter in height, *Striga* produces 50,000 tiny seeds throughout-crossing, thereby accumulating highly heterogenous seed stocks in the soil. In the past few decades, *Striga* has been expanding their geographic territories in vast African farmland over 25 countries and rapidly extending its host range to major crops including maize, millet, upland rice, and an Ethiopian crop called tef as the most recent victim. In severely infested areas, the number of *Striga* seeds reaches up to 15,000 per square meter, enough to completely eliminate crop productions from land that potentially produces 5 tons of maize per hectare. In such cases, smallholder farmers are forced to abandon their farm. The *Striga* endemic in sub-Saharan Africa has been emphasized by the United Nations as a major threat to poverty alleviation, as it economically impacts 10 billion US dollars per year and affects 100 million people. An interdisciplinary team led by researchers from the Institute of Transformative Bio-Molecules (ITbM) at Nagoya University has developed a promising molecule to combat against *Striga*.

Abandoned maize field due to severe infestation by Striga

in Kenya 2018 **Striga seeds**

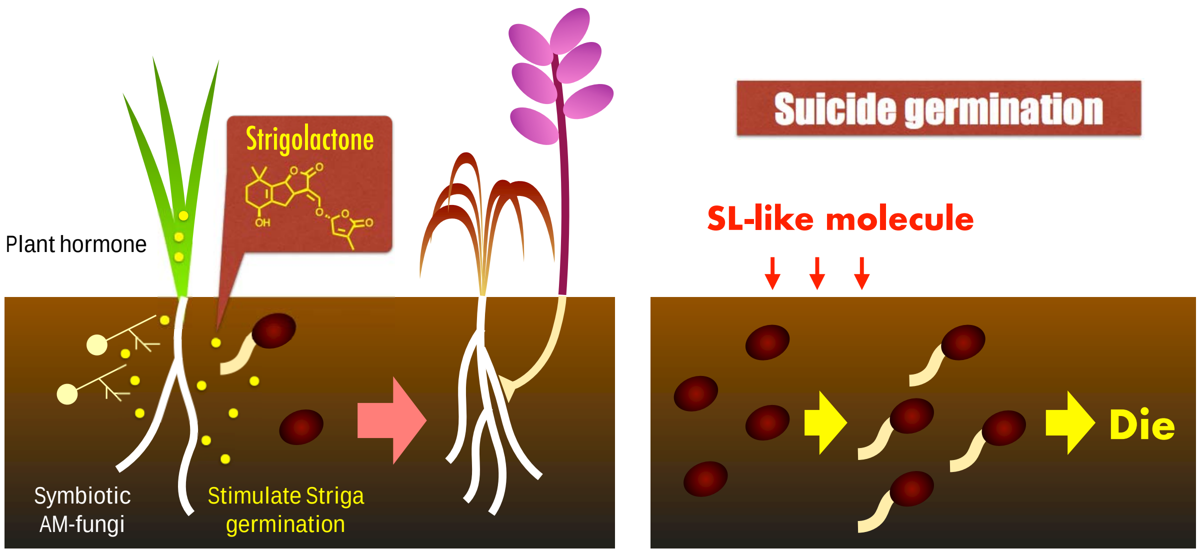
Striga infestation in Africa



G. Ejeta (2007), The Striga scourge in Africa: A growing pandemic.

Infestation of parasitic weed *Striga hermonthica*.

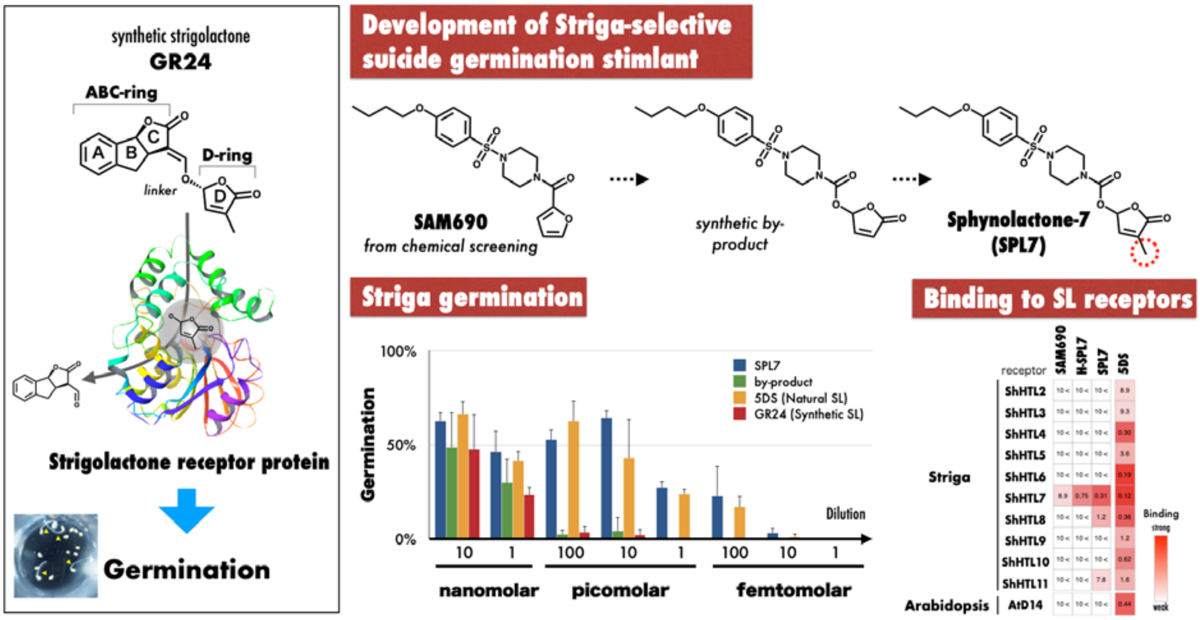
Unlike common plants, seeds of *Striga* stay dormant in the soil over 20 years. The seeds germinate only after they sense a collection of small molecule hormones, strigolactones (SLs), that exude from the host. After germination, the seeds must parasitize the hosts immediately. Otherwise, germinated seeds will use up nutrients stored in the tiny seeds and wither within 4 days. This attribute has prompted researchers to develop SL-like molecules as inducers of suicidal germination to purge the soil of viable *Striga* seeds before planting the crop seed. However, this approach requires the development of potent and accessible compounds that only act on *Striga* and do not impede normal crop development. For example, SLs are also chemical cues that attract root symbiotic arbuscular mycorrhizal fungi (AM fungi) that supply host plants with nutrients. Despite the effort in developing over 300 SL-like molecules in the past 50 years, none of them possess both high potency and *Striga*-selectivity.



Extermination of *Striga* seeds by suicide germination with an SL-like molecule.

The molecular structure of SL is composed of an ABC-ring linked with a D-ring. Upon entering into the pocket of the SL receptor protein, SL is decomposed at the linker site. It has been thought that the structure of the D-ring is important, as it stays in the pocket to activate the receptor and lead *Striga* seeds to germinate. On the other hand, modifying the ABC-portion has been leading the development of variable SL-like molecules. Nonetheless, the exact structure providing *Striga*-selectivity was still unknown. The plant biology team at ITbM led by Yuichiro Tsuchiya initiated the search for a *Striga*-selective molecule from 12,000 synthetic molecules with random structures, and was able to identify a series of hit compounds (represented by a molecule called SAM690) that bind to an SL receptor in *Striga*, but not to that in the model plant *Arabidopsis*, and stimulate *Striga* seed germination with moderate activity (micromolar-range; 10^{-6} M).

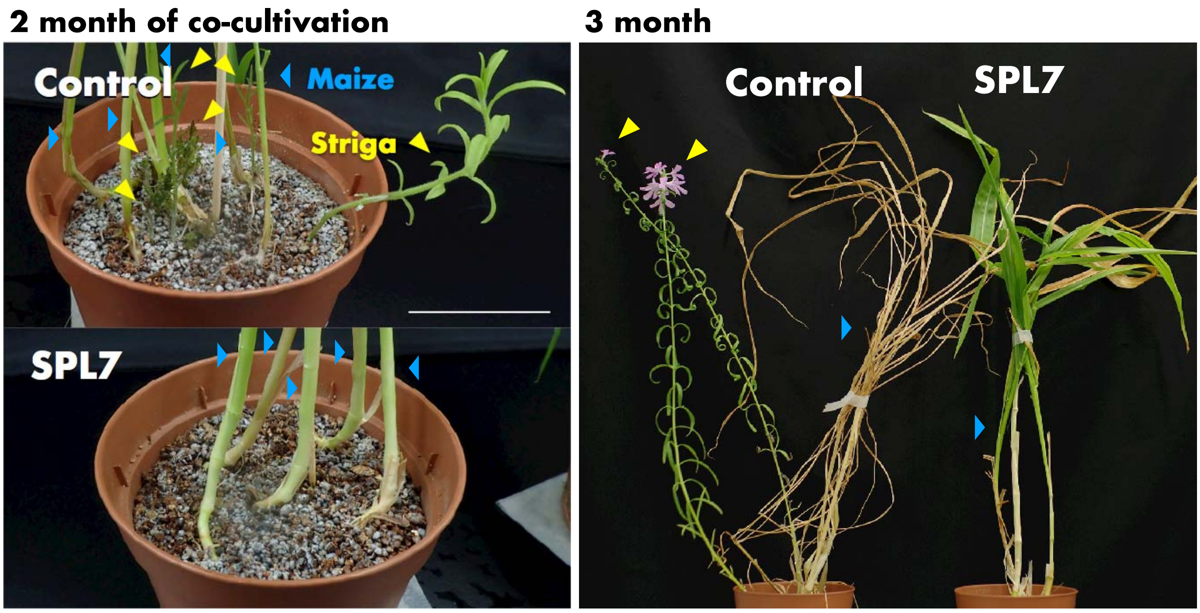
The research went on with a serendipitous discovery of a highly active byproduct generated during the synthesis of hit molecules. The chemistry team led by Daisuke Uraguchi and Takashi Ooi isolated minuscule amount (0.01%) of the byproduct from a crude mixture of a SAM compound and identified its structure as a hybrid of SAM690 and the D-ring component of SLs. The optimized molecule, which is called sphynolactone-7 (SPL7), stimulated *Striga* germination at femtomolar (10^{-15} M) range, yet only bound to the SL receptor in *Striga*. The potency is on par with natural strigolactone, 5-deoxystriogl (5DS), which is the strongest germination stimulant to *Striga* among all commercially available compounds. Named after sphinx (a mystical creature with the head of a lion and the body of a human), SPL7 appeared as a hybrid molecule which inherits *Striga*-selectivity from SAM690 and high potency from SLs.



Development of Striga-selective suicide germination stimulant.

As expected from the selective binding to the SL receptor in *Striga*, SPL7 did not show typical SL activity in Arabidopsis, such as reduction of the number of shoot branches or elongation of root hairs. Not only to Arabidopsis, but SPL7 also appeared to have a limited effect on the growth of AM-fungi, which is an agronomically important microbe. Finally, the research team confirmed that SPL7 did induce suicide germination of *Striga* and protected maize plant from *Striga* parasitism in laboratory experiments. In conclusion, the team has proven that SPL7 is an effective *Striga*-selective suicide germination stimulant at least in laboratory experiments.

ITbM's research team is planning to extend the discovery to field trials of SPL7 in Kenya.



SPL7 induces suicide germination of *Striga* and protects crops

The article “A femto-molar range suicide germination stimulant for the parasitic plant *Striga hermonthica*” by Daisuke Uraguchi, Keiko Kuwata, Yuh Hijikata, Rie Yamaguchi, Hanae Imaizumi Sathiyanarayanan AM, Christin Rakers, Narumi Mori, Kohki Akiyama, Stephan Irle, Peter McCourt, Toshinori Kinoshita, Takashi Ooi, Yuichiro Tsuchiya is published online in *Science*.

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About WPI-ITbM (http://www.itbm.nagoya-u.ac.jp/)
The Institute of Transformative Bio-Molecules (ITbM) at Nagoya University in Japan is committed to advance the integration of synthetic chemistry, plant/animal biology, and theoretical science, all of which are traditionally strong fields in the university. ITbM is one of the research centers of the program initiated by the Japanese Ministry of Education, Culture, Sports, Science and Technology (MEXT), the World Premier International Research Center Initiative (WPI). The aim of ITbM is to develop transformative bio-molecules, innovative functional molecules capable of bringing about fundamental change to biological science and technology. Research at ITbM is carried out in a "Mix Lab" style, where international young researchers from various fields work together side-by-side in the same lab, enabling interdisciplinary interaction. Through these endeavors, ITbM will create "transformative bio-molecules" that will dramatically change the way of research in chemistry, biology and other related fields to solve urgent problems, such as environmental issues, food production and medical technology that have a significant impact on the society.

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