NOVEL POSTTRANSLATIONAL MODIFICATION: GERANYL MODIFICATION ON TRYPtopHAN RESIDUE RESULTING FORMATION OF TRICYCLIC RING STRUCTURE.

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The ComX pheromone is an extracellular signaling molecule that stimulates natural competence controlled by quorum sensing in the Gram-positive bacterium, Bacillus subtilis and related bacilli. The tryptophan residues conserved in the primary sequence of all known ComX pheromones, and are modified by isoprenylation. But the precise structure of the modification was not known.

We determined the structure of the ComXRO-E-2 pheromone, specified by strain RO-E-2 and purified from the broth of Escherichia coli ED413, which was engineered to produce biologically active ComXRO-E-2 pheromone (1). Successively, to confirm the chemical structure we synthesized the modified tryptophan residue and the corresponding ComXRO-E-2 peptide. The synthetic peptide was identical to the natural pheromone, and showed significant activity.

The structure of the ComXRO-E-2 pheromone showed that addition of a geranyl group to a tryptophan residue resulted in the formation of a tricyclic ring structure. This posttranslational geranylation on a tryptophan is a novel modification.

Gly-Ile-Phe-Trp*(Ger)-Glu-Gln
ComXRO-E-2 pheromone

(1) Okada, M.; Sato, I.; Cho, S.J.; Iwata, H.; Nishio, T.; Dubnau D.; Sakagami, Y.