The present invention relates to a process for the expression and secretion in the methylotrophic yeast Pichia pastoris of toxic chimaeric proteins having ribosome-inactivating activity, based on the plant ribosome-inactivating protein (RIP) saporin from soapwort Saponaria officinalis. The invention provides a process for the preparation of recombinant secretory saporin. Such a process comprises the steps of constructing a precursor saporin gene with optimized sequences, inserting the precursor gene into Pichia pastoris GS115 (his4) host strain, followed by fermentation of the transformed clone to obtain secretory recombinant saporin.

Saporin belongs to the N-glycosidase family of plant toxins that includes the prototype RIP ricin: these are ribosome-inactivating proteins able to remove a specific adenine, found in an universally conserved “stem-loop” structure present in ribosomal RNAs from the large ribosome subunit leading to a block in protein synthesis and to apoptotic cell death in eukaryotic intoxicated cells. Toxic domains of RIPs can be coupled to antibody fragments to obtain Immunotoxins, molecules with potential applications to the therapy of tumors.

This expression system is suitable for the production of saporin-based anticancer molecules, but could be also exploited for the production of recombinant toxins (containing saporin) to be used as tools for research purposes (neurobiology).