

Intellectual Property

SemBioSys Genetics' strong intellectual property portfolio ensures the company's worldwide exclusivity to commercialize oleosin/oilbody technology, providing added value to company stakeholders and sustainable competitive advantages to SemBioSys' partners.

The company's technology is protected by the following issued US patents:

- US Patent 7,642,346 – “Flax seed specific promoters”
- US Patent 7,585,645 – “Thioredoxin and thioredoxin reductase containing oil body based products”
- US Patent 7,547,821 – “Methods for the production of insulin in plants”
- US Patent 7,531,325 – “Method for cleavage of fusion proteins”
- US Patent 7,501,265 – “Method for producing and cleaving a fusion protein with an N-terminal chymosin pro-peptide”
- US Patent 7,390,936 – “Commercial production of chymosin in plants”
- US Patent 7,332,587 – “Oil bodies and associated proteins as affinity matrices”
- US Patent 7,093,383 – “Methods for the production of multimeric immunoglobulin, and related compounds”
- US Patent 7,091,401 – “Expression of epidermal growth factor in plant seeds”
- US Patent 6,924,363 - “Oil bodies and associated proteins as affinity matrices”
- US Patent 6,777,591 - "Legume-like storage protein promoter isolated from flax and methods of expressing proteins in plant seeds using the promoter"
- US Patent 6,761,914 - "Immunogenic formulations comprising oil bodies"
- US Patent 6,753,167 - "Preparation of heterologous proteins on oilbodies"
- US Patent 6,750,046 - "Preparation of thioredoxin and thioredoxin reductase proteins on oil bodies"
- US Patent 6,599,513 - "Products for topical applications comprising oilbodies"
- US Patent 6,596,287 - “Products for topical applications comprising oilbodies”
- US Patent 6,582,710 - “Products for topical applications comprising oilbodies”
- US Patent 6,509,453 - "Oilbodies and associated proteins as affinity matrices"
- U.S. Patent 6,372,234 – “Products for topical applications comprising oilbodies”
- U.S. Patent 6,288,304 - "Expression of somatotropin in plant seeds"
- U.S. Patent 6,210,742 - "Uses of oilbodies"
- U.S. Patent 6,183,762 - "Oilbody-based personal care products"
- U.S. Patent 6,146,645 - "Uses of oilbodies"
- U.S. Patent 5,948,682 - "Preparation of heterologous proteins on oilbodies"
- U.S. Patent 5,856,452 - "Oilbodies and associated proteins as affinity matrices"

- U.S. Patent 5,792,922 - "Oilbody protein cis-elements as regulatory signals"
- U.S. Patent 5,650,554 - "Oilbody proteins as carriers of high-value peptides in plants."

In addition the following applications are pending:

- WO 05/047455 – “Methods for the production of apolipoproteins in transgenic plants”
- WO 05/030169 – “Methods for the preparation of oil bodies comprising active ingredients”

Publications

- Markley NA, Nykiforuk CL, Boothe JG and Moloney MM (2006) Producing proteins using transgenic oilbody-oleosin technology. *BioPharm International* 19: 34-57.
- Nykiforuk CL, Boothe JG, Murray EW, Keon RG, Goron, HJ, Markley NA and Moloney MM (2006) Transgenic expression and recovery of biologically active recombinant human insulin from *Arabidopsis thaliana* seeds. *Plant Biotechnology Journal* 4(1): 77-85.
- Bush L (2005) Biotech Processes: Engineered Oilbodies Produce Vaccines and Adjuvants *Pharmaceutical Technology* 29(2): 22.
- Abell BM, Hahn M, Holbrook LA and Moloney MM (2004) Membrane topology and sequence requirements for oil body targeting of oleosin. *The Plant Journal* 37: 461-470.
- Kühnel B, Alcantara J, Boothe J, van Rooijen G and Moloney MM (2003) Precise and efficient cleavage of recombinant fusion proteins using mammalian aspartic proteases. *Protein Engineering* 16(10): 777-783.
- Abell BM, High S and Moloney MM (2002) Membrane Protein Topology of Oleosin is constrained by its long hydrophobic domain. *Journal of Biological Chemistry* 277(10): 8602-8610.
- Boothe JG and Markley NA (2000) The design and use of transgenic plant expression systems for the production of foreign proteins. *Recent Advances in Phytochemistry. Regulation of Phytochemicals by Molecular Techniques* Volume 35, (Eds Romeo JT, Saunders JA and Mathews BF) Pergamon, pp 31-57
- Moloney MM (2000) Molecular farming using seeds as hosts. *In Seeds Technology* (Eds. Bewley D and Black M) Sheffield Academic Press. pp 226-253.
- Moloney MM (2000) Seeds as repositories of recombinant proteins in molecular farming. *Korean Journal of Plant Tissue Culture* 27(4): 283-297.
- Deckers H, Moloney M and Baum A (1999) The case for recombinant production of pharmaceutical proteins in plants. *Annual Reports in Medicinal Chemistry* 34: 237-245

Publications (Cont'd)

- Saborio F, Moloney MM, Tung P and Thorpe TA (1999) Root induction in *Pinus ayacahuite* by co-culture with *Agrobacterium tumefaciens* strains. *Tree Physiology* 19: 383-389
- Ward KA, Tung P, Lamb N, Abrams SR, Reid DM, Moloney MM and Holbrook LA (1999) Structural requirements for biologically active jasmonates: Induction of protease inhibitors and cotyledon senescence. *Plant Growth Regulation* 27: 49-56
- Chaudhary S, Parmenter DL, Moloney MM (1998) Transgenic *Brassica carinata* as a vehicle for the production of recombinant proteins in seeds. *Plant Cell Reports* 17: 195-200
- Kathiresan A, Nagarathna KC, Moloney MM, Reid DM, Chinnappa CC (1998) Differential regulation of 1 aminocyclopropane-1-carboxylate synthase gene family and its role in phenotypic plasticity in *Stellaria longipes*. *Plant Molecular Biology* 36: 265-274
- Kermouni A, Mahmoud SS, Moloney MM, Habibi HR (1998) Cloning of a full-length goldfish Insulin-like growth Factor-I complementary DNA and development of a quantitative PCR method for its measurement *General and Comparative Endocrinology* 111: 51-60
- Layzell DB, Brisson N, Devine MD, Moloney MM, Taylor GJ, Timmer V, Yada RY, Wood K (1998) Plant biology and food science in Canada: a vision for the future. *Canadian Journal of Botany* 76: 355-364
- Mahmoud SS, Wang S, Moloney MM, Habibi HR (1998) Production of a biologically active novel goldfish growth hormone in *Escherichia coli*. *Comparative Biochemistry and Physiology Part B* 120: 657-663
- Moloney MM (1998) Oleosins as carriers for foreign protein in plant seeds. *Engineering Crops for Industrial End Uses*. (Eds Shewry PR, Napier, JA, Davis P), Portland Press. pp47-54
- Abell BM, Holbrook LA, Abenes M, Murphy DJ, Hills MJ, Moloney MM (1997) A novel membrane topology is supported by the oleosin hydrophobic domain which requires a 'proline knot' motif for oil-body incorporation. *Plant Cell* 9: 1481-1493
- Abenes M, Holbrook L, Moloney MM (1997) Transient expression and oilbody targeting of an *Arabidopsis* oleosin-GUS reporter fusion protein in a range of oilseed embryos. *Plant Cell Reports* 17: 1-7
- Boothe JG, Saponja JA, Parmenter DL (1997) Molecular farming in plants: oilseeds as vehicles for the production of pharmaceutical proteins. *Drug Development Research* 42: 172-181
- Holbrook LA, Tung P, Ward KA, Reid DM, Abrams S, Lamb N, Wilson Q, Moloney MM (1997) Importance of the chiral centres of jasmonic acid in the responses of plants: activities and antagonism between natural and synthetic analogues. *Plant Physiology* 114: 419-428
- Liu J-H, Selinger LB, Hu Y-J, Moloney MM, Cheng K-J, Beauchemin KA (1997) An endoglucanase from the anaerobic fungus *Orpinomyces joyonii*: characterization of the gene and its product. *Canadian Journal of Microbiology* 43: 477-485
- Liu J-H, Selinger LB, Cheng K-J, Beauchemin KA, Moloney MM (1997) Plant seed oil-bodies as immobilization matrix for a recombinant xylanase from the rumen fungus *Neocallimastix patriciarum*. *Molecular Breeding* 3: 463-470
- Markley NA, Young D, Laquel P, Castroviejo M and Moloney MM (1997) Molecular genetic and biochemical analysis of *B. napus* PCNA function. *Plant Molecular Biology* 34: 693-700
- Moloney MM, Holbrook LA (1997) Subcellular targeting and purification of recombinant proteins in plant production systems. *Biotechnology and Genetic Engineering Reviews* 14: 321-336
- Hays DB, Rose PA, Abrams SR and Moloney MM (1996) Biological activity of optically pure C-1 altered ABA analogs in *B. napus* microspore embryos. *Journal of Plant Growth Regulation* 15:5-11
- Kuhnel B, Holbrook LA, Moloney MM, and van Rooijen GJH (1996) Oilbodies of transgenic *Brassica napus* as a source of immobilized B-glucuronidase. *Journal of the American Oil Chemists Society* 73(11): 1533-1538
- Mahmoud SS, Moloney MM and Habibi HR (1996) Cloning and sequencing of the goldfish growth hormone cDNA. *General and Comparative Endocrinology* 101: 139-144
- Moloney MM and van Rooijen GJH (1996) Recombinant proteins via oleosin partitioning. *INFORM* 7: 107-113
- Parmenter DL, Boothe JG, Moloney MM (1996) Production and purification of recombinant hirudin from plant seeds. In *Transgenic Plants: A Production System for Industrial and Pharmaceutical Proteins*. (Eds. Owen, M.R.L., Pen, J.) John Wiley & Sons. pp 261-280
- Zhang X-H, Moloney MM, and Chinnappa CC (1996) Analysis of an ABA- and osmotic stress inducible dehydrin from *Stellaria longipes*. *Journal of Plant Physiology* 149: 617-622
- Moloney MM (1995) 'Molecular Farming' in plants: achievements and prospects. *Biotechnology and Biotechnological Equipment* 9/1995/1: 3-9
- Parmenter DL, Boothe JG, van Rooijen GJH, Yeung EC, Moloney MM (1995) Production of biologically active hirudin in plant seeds. *Plant Molecular Biology* 29: 1167-1180.
- Szarka S, Fitch M, Schaerer S and Moloney MM (1995) Classification and expression of a family of cyclin gene homologues in *Brassica napus*. *Plant Molecular Biology* 27: 263-275
- Van Rooijen GJH and Moloney MM (1995) Structural requirements of oleosin domains for subcellular targeting to the oil-body. *Plant Physiology* 109: 1353-1361
- Van Rooijen GJH and Moloney MM (1995) Plant seed oil-bodies as carriers for foreign proteins. *BioTechnology* 13: 72-77
- Plant AL, van Rooijen GJH, Anderson C and Moloney MM (1994) Regulation of an *Arabidopsis* oleosin promoter in transgenic *Brassica napus*. *Plant Molecular Biology* 25: 193-205