Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Review

NMT1 (N-myristoyltransferase 1)

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Published in Atlas Database: November 2010

Online updated version : http://AtlasGeneticsOncology.org/Genes/NMT1ID43604ch17q21.html
DOI: 10.4267/2042/45997

Identity

Other names: NMT

HGNC (Hugo): NMT1

Location: 17q21.31

DNA/RNA

Description

The gene located on the forward strand and spans a size of 47705 bases. It starts at 43138680 and ends at 43186384 bp from pter. The total number of exons is 12.

Transcription

Alternate splicing.

Pseudogene

No known pseudogenes.

Protein

Description

N-myristoyltransferase 1 (NMT 1: EC 2.3.1.97) is a key cellular enzyme which carries out lipid modification by facilitating the attachment of myristate to the N-terminal glycine of several protein molecules. The enzyme's function is indispensible for the growth and development of many eukaryotic organisms and several rotaviruses (Duronio et al., 1989; Duronio et al., 1991; Maurer-Stroh and Eisenhower, 2004; Yang et al., 2005; Wright et al., 2009). The best studied homologue of NMT1 is from the S. cerevisiae (Farazi et al., 2001). It is a monomer and does not require any cofactor or post-translational modifications. The enzyme follows an ordered Bi Bi reaction mechanism in which the apo-enzyme binds myristoyl-CoA to form a NMT1-myristoyl-CoA binary complex which subsequently binds to protein/peptide substrates. The catalytic conversion (N-myristoylation) is via a direct nucleophilic addition-elimination reaction. The sequential release of CoA and myristoyl-peptide follows the formation of an enzyme-product complex from the enzyme-substrate complex (Farazi et al., 2001; Wright et al., 2009). N-myristoyltransferases 1 have a common preference for myristoyl-CoA but have divergent peptide substrate specificities and the enzyme is highly selective for myristoyl-CoA in vitro and in vivo (Farazi et al., 2001). The protein belongs to GNAT superfamily of enzymes and consists of a saddle-shaped beta-sheet flanked by a helices. There is a pseudo two fold symmetry with regions corresponding to N- and C-terminal portions of the enzyme. The N-terminal half forms the myristoyl-CoA binding site whereas the C-terminal half forms the major portion of the peptide binding site (Farazi et al., 2001; Wright et al., 2009). A large number of crystal structures of NMT1 from yeast and human isoforms are available in apo and complex form. Comparative analysis of the various NMTs has shown that the peptide binding pocket is more divergent than the myristoyl-CoA-binding site (Farazi et al., 2001; Wright et al., 2009). Further, the phospho-proteome analysis studies have shown that the human isoform is phosphorylated in vivo at position 47 (Beausoleil et al., 2004; Beausoleil et al., 2006; Olsen et al., 2006;

Dephoure et al., 2008; Mayya et al., 2009). However the biological significance of this observation is not yet established.

Expression

The enzyme is ubiquitous in expression and often exists as isozymes in vivo, varying in either apparent molecular weight and/or subcellular distribution (Selvakumar et al., 2007; Wright et al., 2009). In humans NMT1 is processed to exist as four distinct isoforms ranging from 49 to 68 kDa in size (Giang and Cravatt, 1998). The longer isoform of 496 amino acids represents the full-length protein whereas the shorter isoform represents a translation product of 416 amino acids that initiates with a methionine at amino acid position 81 in the full-length cDNA (Giang and Cravatt, 1998; Farazi et al., 2001). The shorter isoform of NMT1 may arise from an alternative splice variant or through initiation of translation at an internal methionine.

Localisation

NMT1 is a cytoplasmic enzyme because of N-myristoylation being a co-translational protein modification. Recently, it has been reported that the extended N-terminal domain of the longer isoform of NMT1 is involved in targeting the enzyme to the ribosome but it is not required for activity in vitro (Glover et al., 1997). Targeting to the ribosome appears to be consistent with its role as a co-translational protein modifier. In previous studies it has been observed that NMT1 activity from various cell lines and tissues is associated with membranous and particulate fraction (Magnuson et al., 1995; Boutin, 1997). However, the enzyme activity in particulate fractions in earlier studies could represent an association with ribosomes, rather than an authentic membrane association.

Function

N-myristoyltransferase1 catalyses the covalent attachment of myristate, a 14 carbon saturated fatty acid, via amide bond to the N-terminal glycine residue of several proteins (Wright et al., 2009; Hannoush and Sun, 2010). This lipidic modification is an irreversible process, however not without exceptions (Hannoush and Sun, 2010). Intially this process was thought to be co-translational in which the addition of myristate on the N-terminal glycine takes place after initial amino acid residues (within 100) have been synthesized by the ribosome (Wilcox et al., 1987). The process follows after the removal of the initiator methionine by a methionine aminopeptidase to expose an available N-terminal glycine. However, now it has been shown to occur post-translationally as well when an internal glycine within a polypeptide chain is exposed following a proteolytic cleavage (Zha et al., 2000; Utsumi et al., 2003; Martin et al., 2008). The Availability of exposed N-terminal glycine is an absolute requirement and the modification occurs on a general consesus motif of GXXXS/T (where X is any amino acid) (Boutin, 1997; Resh, 1999; Farazi et al., 2001; Wright et al., 2009; Hannoush and Sun, 2010).
Various regular endogenous, physiological enzymes and proteins such as protein kinase A, protein kinase G, NADH-cytochrome b5 reductase, nitric oxide synthase, recoverin, most of the G protein a subunit are the substrates of myristoylation among higher eukaryotes. A detailed list of the substrate proteins is available in a number of reviews elsewhere (Boutin, 1997; Resh, 1999; Maurer-Stroh et al., 2004; Selvakumar et al., 2007). Myristoylation increases protein lipophilicity and is important for the full expression of biological functions of proteins. It controls the functioning of proteins by targeting them to specific localization, promoting specific protein-protein and protein-lipid interactions and ligand-induced conformational changes (Resh, 1999; Farazi et al., 2001; Wright et al., 2009).

Implicated in

Various cancers

Note

Altered NMT expression is observed in many types of cancer tissues including those of colon, breast, gallbladder and brain (Selvakumar et al., 2007; Wright et al., 2009). A quantitative RT-PCR investigation of hNMT-1 expression during the progression of different human cancers shows that hNMT-1 is upregulated in breast, colon, lung and on average by 3.7 ($p=0.032$), 3.1 ($p=0.001$), 2.3 ($p=0.003$) and 1.8 ($p=0.012$) fold, respectively (Chen et al., 2009). These findings are explained by the hypothesis that many of the various proteins/oncoproteins (src, ras etc.) which are overexpressed and activated, during tumorigenesis require myristoylation for their proper function (Boutin, 1997; Resh, 1999; Wright et al., 2009). The elevated NMT activity accounts for the functioning of overexpressed oncoproteins and NMT thus plays a role in cancer progression. The NMT substrate src has elevated activity in human cancers and this contributes to its pathogenicity (Frame, 2002). Inhibiting NMT1 functions has also been shown to reduce proliferation and induce apoptosis in human and murine melanoma cell lines and also to block tumor growth in vivo (Bhandarkar et al., 2008). The siRNA mediated NMT1 knockdown shows that silencing NMT1 inhibits cell replication associated with loss of c-Src activation and its target FAK as well as reduction of various protein kinase regulated pathways (Ducker et al., 2005). The knockdown of either of the isozymes, NMT1 or NMT2 results in apoptosis with NMT2 having a more pronounced effect than NMT1. However, in a mouse model the intratumoral injection mainly of NMT1 siRNA has been shown to be responsible for inhibition of tumor growth (Ducker et al., 2005). It has been concluded that among the two isoforms of NMT

(NMT1 and NMT2), both have only partially overlapping functions and that NMT1 is critical for tumor cell proliferation further suggesting that isoform-specific inhibitors might be developed as potential anti-cancer agents (Ducker et al., 2005). It is now apparent that NMT represents both a valuable clinical marker and therapeutic target for cancer (Boutin, 1997; Ducker et al., 2005; Selvakumar et al., 2007; Wright et al., 2009). A several fold increase in NMT activity in polyps and stage B1 tumors compared to normal colonic mucosa have been proposed to be used as a diagnostic/prognostic tool for early detection of colorectal cancer (Raju et al., 1997; Shrivastav et al., 2007; Kumar et al., 2011).

Colorectal cancer

Disease

Colorectal cancer is associated with significantly high mortality and is one of the most common forms of malignancy world wide (Segal and Saltz, 2009). In the western world, it accounts for the second most common cause of cancer associated deaths (Midgley and Kerr, 2001; Tol and Punt, 2010) and is the fourth most common cause of malignancy in the United States (Wolpin et al., 2007; Wolpin and Mayer, 2008). A majority of colon cancer develop from the pre-cancerous polyps on the lining of the colon which grow over the years to becomes cancerous in nature (Midgley and Kerr, 1999). With the increasing armentarium towards colon cancer (Midgley and Kerr, 1999; Midgley and Kerr, 2001; Wolpin et al., 2007; Wolpin and Mayer, 2008; Segal and Saltz, 2009; Tol and Punt, 2010), it is one of the most curable forms of cancer if detected early. However, due to the lack of early symptoms, the majority of the patients have an advanced disease at presentation (Midgley et al., 2001; Segal and Saltz, 2009). Studies have shown that NMT represents both a valuable marker for clinical diagnosis and as a therapeutic target for colon cancer (Magnuson et al., 1995; Raju et al., 1997; Shrivastav et al., 2007; Kumar et al., 2011).

Prognosis

A direct relationship has been reported for NMT expression and activity and colon cancer progression (Magnuson et al., 1995; Raju et al., 1997). NMT activity and expression has been shown to be upregulated during the progression of colorectal cancer (Magnuson et al., 1995; Raju et al., 1997) and NMT thus has been proposed as a potential chemotherapeutic target (Felsted et al., 1995). A significantly higher NMT activity in rat colonic tumors and a several fold increase in NMT activity in polyps and stage B1 tumors compared to normal colonic mucosa have indicated that NMT could be used as a diagnostic/prognostic tool for colorectal cancer (Magnuson et al., 1995; Raju et al., 1997; Shrivastav et al., 2007). Altered expression and localization of NMT in the peripheral blood and bone marrow of colon cancer patients have offered an advantage for early detection of colorectal cancer using NMT as a blood based marker (Shrivastav et al., 2007; Kumar et al., 2011). The immunohistochemical analysis shows weak to negative staining for NMT in peripheral blood mononuclear cells (PBMC) of controls, whereas strong positivity is observed in the PBMC of colon cancer patients (Shrivastav et al., 2007; Kumar et al., 2011). In addition, NMT is confined mostly in the nuclei of the bone marrow (BM) mononuclear cells of the colon cancer patients, whereas in the control bone marrow specimens it remained cytoplasmic. The strikingly different NMT expression and its altered localization offers the basis of a potential adjunct investigative tool for screening or diagnosis of patients at risk for, or suspected of having, colon cancer (Shrivastav et al., 2007; Kumar et al., 2011). It has been observed that in colon cancer cell lines, an elevated expression of NMT correlates with high levels of c-Src levels (Rajala et al., 2000a). Further it has been observed that the levels of the myristoylated tyrosine kinases, $pp60^{c\text{-}src}$ and $pp60^{c\text{-}yes}$ are several fold higher in colonic preneoplastic lesions and neoplasms compared with normal colon cells (Bolen et al., 1987; Weber et al., 1992; Termuhlen et al., 1993). Differential expression of $pp60^{c\text{-}src}$ has been observed in colonic tumor-derived cell lines (Bolen et al., 1987; Weber et al., 1992) and colonic polyps prone to developing cancer (Cartwright et al., 1990). In the intestinal crypt cells, higher levels of cytoskeletal-associated $pp60^{c\text{-}src}$ protein tyrosine kinase activity have been observed along with higher expression of $pp60^{c\text{-}yes}$ in the normal intestinal epithelium (Zhao et al., 1990; Cartwright et al., 1993). Studies have revealed that $pp60^{c\text{-}src}$ is overexpressed in human colon carcinoma and it has enhanced kinase activity in progressive stages and metastases of human colorectal cancer (Bolen et al., 1987; Termuhlen et al., 1993). Furthermore, it has been shown that src kinase activity is positively regulated by myristoylation and the non-myristoylated c-Src exhibited has reduced kinase activity (Patwardhan and Resh, 2010). The blockages of $pp60^{c\text{-}src}$ N-myristoylation in colonic cell lines have been reported to result in depressed colony formation and reduced proliferation (Shoji et al., 1990).

Gallbladder cancer

Disease

Gallbladder cancer, also known as carcinoma of the gallbladder, is extremely rare affecting the gall bladder (the organ behind the liver which stores bile
produced by the liver). Gallbladder is a non-essential organ and can be removed without significant consequences. However, since gallbladder cancer is very uncommon and many of its symptoms are similar to those of more common ailments (jaundice, pain, and fever), cancer of the gallbladder is usually not found until it is at an advanced stage and cannot be surgically removed.

Prognosis

Gallbladder cancer tends to spread to the liver or small intestine and also spreads to lymph nodes through the lymphatic system in the region of the liver resulting in involvement of other lymph nodes and organs. The treatments available are not particularly effective, unless the tumor is very small and found in which case the gallbladder is removed for other reasons. A study of documented gallbladder carcinoma cases has been evaluated for NMT and p53 expression by immunohistochemistry in both in situ and in invasive tumor components (Rajala et al., 2000b). Moderate to strong cytoplasmic positivity for NMT with increased intensity in the invasive component was observed in 60% of the cases. A mild to moderate cytoplasmic staining was revealed in the in situ component in 67% of the cases studied. It has been concluded that increased NMT expression in gall bladder tumors is associated with poor clinical outcomes as evidenced by their mean survival times (Rajala et al., 2000b).

Breast cancer

Disease

Breast cancer originates from the breast tissue, most commonly from the inner lining of milk ducts (ductal carcinoma) or the lobules (lobular carcinoma) that supply the ducts with milk. It is the fifth most common cause of cancer death and comprises 10.4% of all cancer incidences among women worldwide, and is the most common type of non-skin cancer in women.

Prognosis

It has been observed that in the mammary epithelial cells, the proliferative capacity correlates with NMT activity (Clegg et al., 1999). A study of the NMT profiles in tumourigenic or metastatic breast cancer cell lines have displayed reduced NMT activity and western blot analysis shows that NMT1 is phosphorylated in these breast cancer cells (Shrivastav et al., 2009). Furthermore, patients' breast cancer tissue array revealed strong positivity and high intensity for NMT in malignant breast tissues compared with normal breast cells. In the grade I, II, and III infiltrating ductal carcinoma breast tissues, a gradation in the NMT staining was observed (Shrivastav et al., 2009). It has been concluded that NMT may prove to be an additional diagnostic biomarker for breast cancer.

HIV infection

Disease

The human immunodeficiency virus (HIV) is a member of the retrovirus family (lentivirus) that causes acquired immune deficiency syndrome (AIDS). In this syndrome the immune system begins to fail leading to life-threatening opportunistic infections. The major routes of infections are via the transfer of blood, breast milk, semen, vaginal fluid and the pre-ejaculate. If left untreated, the progressive failure of the immune system results in opportunistic infections or malignancies leading to the death of individuals in most of the cases.

Prognosis

The pathogenic states linked to undesired myristoylation activity includes the myristoylation of viral proteins for their proper maturation and infectivity (Boutin, 1997; Maurer-Stroh and Eisenhower, 2004; Wright et al., 2009). Many of the viral genes are homologues of the tyrosine kinases and require N-myristoylation for the infectivity of viral particles. In the case of HIV infections, viral proteins Gag and Nef require myristoylation by the host cell NMT to carry out their function properly. Gag is the precursor polyprotein for structural components of the viral capsid and requires myristoylation for intracellular localization and its targeting to the lipid rafts in the plasma membrane during virus assembly (Zhou et al., 1994; Resh, 2004; Wright et al., 2009). Nef on the other hand comprises many virulence factors to modify the cellular environment of infected cells to facilitate viral replication and evade detection by cells of the immune system (Collins et al., 1998). It has been reported that NMT1 myristoylates Gag in vivo and inhibiting NMT1 negatively affects HIV production (Takamune et al., 2008).

References

Bolen JB, Veillette A, Schwartz AM, DeSeau V, Rosen N. Activation of pp60c-src protein kinase activity in human colon carcinoma. Proc Natl Acad Sci U S A. 1987 Apr;84(8):2251-5

Wilcox C, Hu JS, Olson EN. Acylation of proteins with myristic acid occurs cotranslationally. Science. 1987 Nov 27;238(4831):1275-8

Duronio RJ, Towler DA, Heuckeroth RO, Gordon JI. Disruption of the yeast N-myristoyl transferase gene causes recessive lethality. Science. 1989 Feb 10;243(4892):796-800

Cartwright CA, Meisler AI, Eckhart W. Activation of the pp60c-src protein kinase is an early event in colonic carcinogenesis. Proc Natl Acad Sci U S A. 1990 Jan;87(2):558-62

Shoji S, Kurosawa T, Inoue H, Funakoshi T, Kubota Y. Human cellular src gene product: identification of the myristoylated pp60c-src and blockage of its myristoyl acylation with N-fatty acyl compounds resulted in the suppression of colony formation. Biochem Biophys Res Commun. 1990 Dec 31;173(3):894-901

Zhao YH, Krueger JG, Sudol M. Expression of cellular-yes protein in mammalian tissues. Oncogene. 1990 Nov;5(11):1629-35

Duronio RJ, Rudnick DA, Johnson RL, Johnson DR, Gordon JI. Myristic acid auxotrophy caused by mutation of S. cerevisiae myristoyl-CoA:protein N-myristoyltransferase. J Cell Biol. 1991 Jun;113(6):1313-30

Weber TK, Steele G, Summerhayes IC. Differential pp60c-src activity in well and poorly differentiated human colon carcinomas and cell lines. J Clin Invest. 1992 Sep;90(3):815-21

Cartwright CA, Mamajiwalla S, Skolnick SA, Eckhart W, Burgess DR. Intestinal crypt cells contain higher levels of

cytoskeletal-associated pp60c-src protein tyrosine kinase activity than do differentiated enterocytes. Oncogene. 1993 Apr;8(4):1033-9

Termuhlen PM, Curley SA, Talamonti MS, Saboorian MH, Gallick GE. Site-specific differences in pp60c-src activity in human colorectal metastases. J Surg Res. 1993 Apr;54(4):293-8

Zhou W, Parent LJ, Wills JW, Resh MD. Identification of a membrane-binding domain within the amino-terminal region of human immunodeficiency virus type 1 Gag protein which interacts with acidic phospholipids. J Virol. 1994 Apr;68(4):2556-69

Felsted RL, Glover CJ, Hartman K. Protein N-myristoylation as a chemotherapeutic target for cancer. J Natl Cancer Inst. 1995 Nov 1;87(21):1571-3

Magnuson BA, Raju RV, Moyana TN, Sharma RK. Increased N-myristoyltransferase activity observed in rat and human colonic tumors. J Natl Cancer Inst. 1995 Nov 1;87(21):1630-5

Boutin JA. Myristoylation. Cell Signal. 1997 Jan;9(1):15-35

Glover CJ, Hartman KD, Felsted RL. Human N-myristoyltransferase amino-terminal domain involved in targeting the enzyme to the ribosomal subcellular fraction. J Biol Chem. 1997 Nov 7;272(45):28680-9

Raju RV, Moyana TN, Sharma RK. N-Myristoyltransferase overexpression in human colorectal adenocarcinomas. Exp Cell Res. 1997 Aug 25;235(1):145-54

Collins KL, Chen BK, Kalams SA, Walker BD, Baltimore D. HIV-1 Nef protein protects infected primary cells against killing by cytotoxic T lymphocytes. Nature. 1998 Jan 22;391(6665):397-401

Giang DK, Cravatt BF. A second mammalian N-myristoyltransferase. J Biol Chem. 1998 Mar 20;273(12):6595-8

Clegg RA, Gordge PC, Miller WR. Expression of enzymes of covalent protein modification during regulated and dysregulated proliferation of mammary epithelial cells: PKA, PKC and NMT. Adv Enzyme Regul. 1999;39:175-203

Midgley R, Kerr D. Colorectal cancer. Lancet. 1999 Jan 30;353(9150):391-9

Resh MD. Fatty acylation of proteins: new insights into membrane targeting of myristoylated and palmitoylated proteins. Biochim Biophys Acta. 1999 Aug 12;1451(1):1-16

Rajala RV, Dehm S, Bi X, Bonham K, Sharma RK. Expression of N-myristoyltransferase inhibitor protein and its relationship to c-Src levels in human colon cancer cell lines. Biochem Biophys Res Commun. 2000a Jul 14;273(3):1116-20

Rajala RV, Radhi JM, Kakkar R, Datla RS, Sharma RK. Increased expression of N-myristoyltransferase in gallbladder carcinomas. Cancer. 2000b May 1;88(9):1992-9

Zha J, Weiler S, Oh KJ, Wei MC, Korsmeyer SJ. Posttranslational N-myristoylation of BID as a molecular switch for targeting mitochondria and apoptosis. Science. 2000 Dec 1;290(5497):1761-5

Farazi TA, Waksman G, Gordon JI. The biology and enzymology of protein N-myristoylation. J Biol Chem. 2001 Oct 26;276(43):39501-4

Midgley R, Kerr D. Conventional cytotoxic and novel therapeutic concepts in colorectal cancer. Expert Opin Investig Drugs. 2001 Jun;10(6):1011-9

Frame MC. Src in cancer: deregulation and consequences for cell behaviour. Biochim Biophys Acta. 2002 Jun 21;1602(2):114-30

Utsumi T, Sakurai N, Nakano K, Ishisaka R. C-terminal 15 kDa fragment of cytoskeletal actin is posttranslationally N-myristoylated upon caspase-mediated cleavage and targeted to mitochondria. FEBS Lett. 2003 Mar 27;539(1-3):37-44

Beausoleil SA, Jedrychowski M, Schwartz D, Elias JE, Villén J, Li J, Cohn MA, Cantley LC, Gygi SP. Large-scale characterization of HeLa cell nuclear phosphoproteins. Proc Natl Acad Sci U S A. 2004 Aug 17;101(33):12130-5

Maurer-Stroh S, Eisenhaber F. Myristoylation of viral and bacterial proteins. Trends Microbiol. 2004 Apr;12(4):178-85

Maurer-Stroh S, Gouda M, Novatchkova M, Schleiffer A, Schneider G, Sirota FL, Wildpaner M, Hayashi N, Eisenhaber F. MYRbase: analysis of genome-wide glycine myristoylation enlarges the functional spectrum of eukaryotic myristoylated proteins. Genome Biol. 2004;5(3):R21

Resh MD. A myristoyl switch regulates membrane binding of HIV-1 Gag. Proc Natl Acad Sci U S A. 2004 Jan 13;101(2):417-8

Ducker CE, Upson JJ, French KJ, Smith CD. Two N-myristoyltransferase isozymes play unique roles in protein myristoylation, proliferation, and apoptosis. Mol Cancer Res. 2005 Aug;3(8):463-76

Yang SH, Shrivastav A, Kosinski C, Sharma RK, Chen MH, Berthiaume LG, Peters LL, Chuang PT, Young SG, Bergo MO. N-myristoyltransferase 1 is essential in early mouse development. J Biol Chem. 2005 May 13;280(19):18990-5

Beausoleil SA, Villén J, Gerber SA, Rush J, Gygi SP. A probability-based approach for high-throughput protein phosphorylation analysis and site localization. Nat Biotechnol. 2006 Oct;24(10):1285-92

Olsen JV, Blagoev B, Gnad F, Macek B, Kumar C, Mortensen P, Mann M. Global, in vivo, and site-specific phosphorylation dynamics in signaling networks. Cell. 2006 Nov 3;127(3):635-48

Selvakumar P, Lakshmikuttyamma A, Shrivastav A, Das SB, Dimmock JR, Sharma RK. Potential role of N-myristoyltransferase in cancer. Prog Lipid Res. 2007 Jan;46(1):1-36

Shrivastav A, Varma S, Saxena A, DeCoteau J, Sharma RK. N-myristoyltransferase: a potential novel diagnostic marker for colon cancer. J Transl Med. 2007 Nov 16;5:58

Wolpin BM, Meyerhardt JA, Mamon HJ, Mayer RJ. Adjuvant treatment of colorectal cancer. CA Cancer J Clin. 2007 May-Jun;57(3):168-85

Bhandarkar SS, Bromberg J, Carrillo C, Selvakumar P, Sharma RK, Perry BN, Govindarajan B, Fried L, Sohn A, Reddy K, Arbiser JL. Tris (dibenzylideneacetone) dipalladium, a N-myristoyltransferase-1 inhibitor, is effective against melanoma growth in vitro and in vivo. Clin Cancer Res. 2008 Sep 15;14(18):5743-8

Dephoure N, Zhou C, Villén J, Beausoleil SA, Bakalarski CE, Elledge SJ, Gygi SP. A quantitative atlas of mitotic phosphorylation. Proc Natl Acad Sci U S A. 2008 Aug 5;105(31):10762-7

Martin DD, Vilas GL, Prescher JA, Rajaiah G, Falck JR, Bertozzi CR, Berthiaume LG. Rapid detection, discovery, and identification of post-translationally myristoylated proteins during apoptosis using a bio-orthogonal azidomyristate analog. FASEB J. 2008 Mar;22(3):797-806

Seaton KE, Smith CD. N-Myristoyltransferase isozymes exhibit differential specificity for human immunodeficiency virus type 1 Gag and Nef. J Gen Virol. 2008 Jan;89(Pt 1):288-96

Takamune N, Gota K, Misumi S, Tanaka K, Okinaka S, Shoji S. HIV-1 production is specifically associated with human NMT1 long form in human NMT isozymes. Microbes Infect. 2008 Feb;10(2):143-50

Wolpin BM, Mayer RJ. Systemic treatment of colorectal cancer. Gastroenterology. 2008 May;134(5):1296-310

Chen L, Ling B, Alcorn J, Yang J.. Quantitative Analysis of the Expression of Human N-myristoyltransferase 1 (hNMT-1) in Cancers. The open Biomarker Journal. 2009; 2: 6-10.

Mayya V, Lundgren DH, Hwang SI, Rezaul K, Wu L, Eng JK, Rodionov V, Han DK.. Quantitative phosphoproteomic analysis of T cell receptor signaling reveals system-wide modulation of protein-protein interactions. Sci Signal. 2009 Aug 18;2(84):ra46.

Segal NH, Saltz LB.. Evolving treatment of advanced colon cancer. Annu Rev Med. 2009;60:207-19. (REVIEW)

Shrivastav A, Varma S, Senger A, Khandelwal RL, Carlsen S, Sharma RK.. Overexpression of Akt/PKB modulates N-myristoyltransferase activity in cancer cells. J Pathol. 2009 Jul;218(3):391-8.

Wright MH, Heal WP, Mann DJ, Tate EW.. Protein myristoylation in health and disease. J Chem Biol. 2009 Nov 7. (Epub ahead of print)

Hannoush RN, Sun J.. The chemical toolbox for monitoring protein fatty acylation and prenylation. Nat Chem Biol. 2010 Jul;6(7):498-506. (REVIEW)

Patwardhan P, Resh MD.. Myristoylation and membrane binding regulate c-Src stability and kinase activity. Mol Cell Biol. 2010 Sep;30(17):4094-107. Epub 2010 Jun 28.

Tol J, Punt CJ.. Monoclonal antibodies in the treatment of metastatic colorectal cancer: a review. Clin Ther. 2010 Mar;32(3):437-53. (REVIEW)

Kumar S, Dimmock JR, Sharma RK.. N-Myristoyltransferase in Colon Cancer: A New Marker for Early Diagnosis. Cancers (2011) (Special Issue "Cancer Diagnosis and Targeted Therapy). (Invited review, Manuscript in preparation)

This article should be referenced as such:

Selvakumar P, Kumar S, Dimmock JR, Sharma RK. NMT1 (N-myristoyltransferase 1). Atlas Genet Cytogenet Oncol Haematol. 2011; 15(7):570-575.