Cambridge Isotope Laboratories, Inc.
www.isotope.com

RESEARCH PRODUCTS

Stable Isotopes for Quantitative Proteomics

Metabolic Labeling

- New! SILAC Protein Quantitation Kits
- New! MouseExpress™ Stable Isotope Labeled Mouse Feed
- New! MouseExpress™ Stable Isotope Labeled Mouse Tissue
- New! 99% Enriched Amino Acids

Enzymatic Labeling

Protected Amino Acids

Chemical Labeling

The Use of Stable Isotopes in Quantitative Proteomics

Over the past decade, there have been vast improvements in the detection and quantification of proteins using LC-MS methodologies. Advancements in the field of bio-informatics, along with the increasing advantages in the use of stable isotopes, has allowed the development of quantitative methods that are capable of simultaneously measuring hundreds or even thousands of proteins in a given biological sample. The field of MS-based Quantitative Proteomics has matured to a point that it is now routine to undergo quantitative, comparative investigations into the proteome to better understand disease and to search for potential protein biomarkers. Although some quantitative measurements can be made without the use of stable isotopes, the use of labeled samples, in conjunction with mass spectrometry, generally increases the accuracy of the quantitative results; saves time by requiring fewer experimental replicates; and requires less sophisticated and thus less expensive instrumentation.

The utility of stable isotopes has helped initiate a variety of different isotopic labeling methods presently used in proteomics. **Metabolic labeling** experiments mix samples and controls together in known amounts, where one is enriched in stable isotopes. This method can be performed in cells as well as higher organisms, such as insects, fish, and mammals. A main advantage of this method is that samples are mixed at the onset of the sample preparation workflow, thus automatically correcting for possible fractionation during workup. Perhaps the most important feature of metabolic labeling is that the label is introduced into the proteome *in vivo*, which represents the most meaningful possible "snapshot" of the proteome for investigation.

Enzymatic labeling, a well established strategy utilizing ^{18}O water, is accomplished by performing a digestion using a specific enzyme such as trypsin or Lys-C in the presence of ^{18}O water. This method incorporates the ^{18}O isotope into the carboxy terminus of the peptides, increasing the mass by 2 or 4 Da, thus allowing the isotope labeled peptides to be identified by mass spectrometry. In addition, **chemical labeling** methods employ externally introduced tags. These methods exploit the available functional groups in proteins and peptides, allowing for the introduction of isotope enriched "tagging reagents" using standard chemistry techniques. The common feature among these proteomic methods is that stable isotopes provide for the quantitation (relative or absolute) of proteins, based upon a well characterized increase in molecular mass in the protein or peptide of interest.

CIL offers many products that are used in the field of proteomics such as our unique MouseExpress™ Mouse Feed Labeling Kit (Lysine, $^{13}C_6$, 99%), Spirulina (^{15}N, 98%), MouseExpress™ Mouse Tissue (Lysine $^{13}C_6$, 97%), SILAC Protein Quantitation Kits, 99% enriched amino acids (^{13}C and $^{13}C/^{15}N$), protected amino acids for peptide synthesis, ^{18}O and ^{17}O water for enzymatic labeling, and growth media components and reagents suitable for bacterial, insect, yeast and mammalian cell culture. In addition, we offer an assortment of reagents for chemical tagging of peptides and proteins.

Our commitment to support innovation in scientific fields, as well as continuously striving to exceed our customers' expectations, has allowed us numerous opportunities to respond to the changing demands of the many research applications which utilize stable isotope labeled compounds.

CIL is pleased to introduce our 2010 **Stable Isotopes for Quantitative Proteomics** brochure. Included are technical excerpts from some of the leaders in this dynamic field and a comprehensive listing of reagents utilized in a variety of proteomic methodologies.

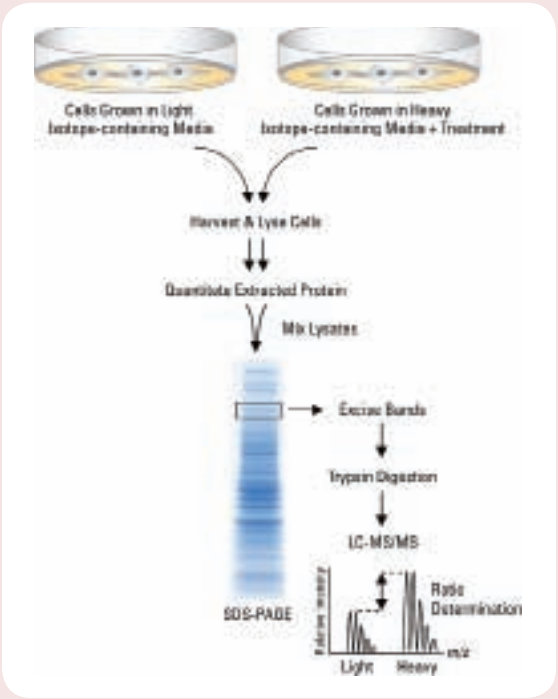
We welcome your comments and suggestions on new products and ways we can better assist you in your research.

Metabolic Labeling

Stable Isotope Labeling with Amino Acids in Cell Culture (SILAC)

Stable isotope labeling with amino acids in cell culture (SILAC) is a simple and straightforward approach for *in vivo* incorporation of a label into proteins for mass spectrometry (MS)-based quantitative proteomics. SILAC relies on metabolic incorporation of a given 'light' (unlabeled) or 'heavy' (labeled) form of the amino acid into the proteins. The method relies on the incorporation of amino acids with substituted stable isotopic nuclei (e.g. ^{13}C, ^{15}N). Thus in an experiment, two cell populations are grown in culture media that are identical except that one of them contains a 'light' and the other a 'heavy' form of a particular amino acid (e.g. ^{12}C and ^{13}C labeled L-Lysine, respectively). When the labeled analog of an amino acid is supplied to cells in culture instead of the natural amino acid, it is incorporated into all newly synthesized proteins. After a number of cell divisions, each instance of this particular amino acid will be replaced by its isotope labeled analog. Since there is hardly any chemical difference between the labeled amino acid and the natural amino acid isotopes, the cells behave exactly like the control cell population grown in the presence of normal amino acid. It is efficient and reproducible as the incorporation of the isotope label is 100%. We anticipate that potential applications of SILAC will lead to its use as a routine technique in all areas of cell biology.

- Dr. Akhilesh Pandey
Johns Hopkins University



Example of SILAC workflow

SILAC Highlights:

- **Efficient** -100% label incorporation into proteins of cultured cells
- **Reproducible** - eliminates experimental variability caused by differential sample preparation
- **Flexible** - media deficient in both L-Lysine and L-Arginine, allowing for better proteome coverage through dual amino acid isotope labeling
- **Compatible** - label proteins expressed in a wide variety of mammalian cell lines adapted to grow in DMEM or RPMI 1640 medium, including HeLa, 293T, COS7, U2OS, A549, A431, HepG2, NIH 3T3, Jurkat and others

SILAC Applications:

- Quantitative analysis of relative changes in protein abundance from different cell treatments
- Quantitative analysis of proteins for which antibodies are unavailable
- Protein expression profiling of normal vs. disease cells
- Identification and quantification of hundreds to thousands of proteins in a single experiment

New! SILAC Protein Quantitation Kits

Kit contains:
- DMEM or RPMI 1640 Media for SILAC, 2 x 500 mL
- Dialyzed FBS, 2 x 50 mL
- L-Lysine•2HCl (U-$^{13}C_6$, 97-99%), 50 mg
- L-Lysine•2HCl, 50 mg
- L-Arginine•HCl, 2 x 50 mg

Media (DMEM or RPMI 1640), Dialyzed FBS, and amino acids are also sold separately.

*SILAC Media and Dialyzed FBS are manufactured by Thermo Fisher Scientific, Inc. SILAC Media is provided by Thermo Fisher Scientific under license from the University of Washington and protected by U.S. Patent 6,653,076, for research use only.

New! SILAC Protein Quantitation Kits

Catalog No.	Description
DMEM-LYS-C	**SILAC Protein Quantitation Kit DMEM (Dulbecco's Modified Eagle Media)**

Kit contains:
- SILAC DMEM Media, 2 x 500 mL
- Dialyzed FBS, 2 x 50 mL
- L-Lysine•2HCl (U-$^{13}C_6$, 97-99%), 50 mg
- L-Lysine•2HCl, 50 mg
- L-Arginine•HCl, 2 x 50 mg

Catalog No.	Description
RPMI-LYS-C	**SILAC Protein Quantitation Kit RPMI 1640**

Kit contains:
- SILAC RPMI 1640 Media, 2 x 500 mL
- Dialyzed FBS, 2 x 50 mL
- L-Lysine•2HCl (U-$^{13}C_6$, 97- 99%), 50 mg
- L-Lysine•2HCl, 50 mg
- L-Arginine•HCl, 2 x 50 mg

New! Additional Products

Catalog No.	Description
DMEM-500	**DMEM Media for SILAC (DMEM minus L-Lysine and L-Arginine)**
RPMI-500	**RPMI 1640 Media for SILAC (RPMI 1640 minus L-Lysine and L-Arginine)**
FBS-50	**Dialyzed Fetal Bovine Serum**

SILAC Literature References

Ong, S.E., Blagoev, B., Kratchmarova, I., Kristensen, D.B., Steen. H., Pandey. A., Mann, M. **2002.** Stable isotope labeling by amino acids in cell culture, SILAC, as a simple and accurate approach to expression proteomics. Mol Cell Proteomics, 1*(5)*, 376-386.

Amanchy, R., Kalume. D.E., Pandey, A. **2005.** Stable isotope labeling with amino acids in cell culture (SILAC) for studying dynamics of protein abundance and posttranslational modifications. Sci STKE, 267, 1-20.

Blagoev, B., Ong, S.E., Kratchmarova. I., Mann. M. **2004.** Temporal analysis of phosphotyrosine-dependent signaling networks by quantitative proteomics. Nature Biotechnology, 22*(9)*, 1139-1145.

Kratchmarova, I., Blagoev. B., Haack-Sorensen. M., Kassem, M., Mann, M. **2005.** Mechanism of divergent growth factor effects in mesenchymal stem cell differentiation. Science, 308*(5727)*, 1472-1477.

Mann, M. **2006.** Functional and quantitative proteomics using SILAC. Nat Rev Mol Cell Biol, 7*(12)*, 952-958.

Selbach, M., Mann, M. **2006.** Protein interaction screening by quantitative immunoprecipitation combined with knockdown (QUICK). Nature Methods, 3*(12)*, 981-983

Stable Isotope Labeling in Mammals (SILAM)

As SILAC is limited to cell culture, investigations at the tissue, organ or whole animal level require a different methodology. Stable Isotope Labeling in Mammals (SILAM) has been achieved utilizing ^{13}C as well as ^{15}N. Spirulina ^{15}N has been used to uniformly label the proteome with ^{15}N. Animal models of human disease provide a powerful system for the study of molecular mechanisms associated with disease. A quantitative proteomic method for the study of *in vivo* biology using ^{15}N Stable Isotope Labeling in Mammals (SILAM) has been created through stable isotope labeling of the rats and mice (1). Food is prepared using the algae *Arthrospira platensis* (also commonly called Spirulina) grown on ^{15}N to incorporate the stable isotope into all proteins. By combining ^{15}N Spirulina with a protein free chow, food is created that provides only ^{15}N labeled protein with the other nutrients and vitamins required for normal growth (1-3). This method of stable isotope labeling uses the synthetic machinery of the cell to incorporate ^{15}N into proteins and as a result it is a comprehensive technique for cell and tissue labeling. **Labeled tissues can then be used as an internal standard when mixed with the diseased tissues from an animal model for a disease.** By using "shotgun proteomics" (Figure 1) mixtures of the intact proteins are proteolytically digested and then analyzed by two-dimensional liquid chromatography coupled to a tandem mass spectrometer (4). A tandem mass spectrometer can rapidly analyze peptides by generating fragmentation patterns for individual peptides in the mixture. Tandem mass spectra collected for peptides are then used as an "address" or "zip code" to identify proteins in sequence databases (5). Peptides serve as a surrogate for the intact proteins and are used to identify a protein's presence, and through the stable isotope labeling process, to measure changes in protein expression. By introducing ^{15}N labeled amino acids into proteins, a "heavier" version of a protein is produced that can be readily differentiated from ^{14}N labeled proteins (e.g. light) by a mass spectrometer. Thus, if a "heavy" normal mouse (control) is compared to a "light" diseased mouse, the differences in protein expression between the two can be determined using shotgun proteomics and mass spectrometry. This process will allow the discovery of pathways or processes that are up- or down-regulated as a function of disease.

– Dr. John Yates
The Scripps Research Institute

References

1. Wu, C.C., MacCoss, M.J., Howell, K.E., Matthews, D.E., and Yates, J.R., 3rd **2004**. Metabolic labeling of mammalian organisms with stable isotopes for quantitative proteomic analysis. Anal Chem *76*, 4951-4959.
2. McClatchy, D.B., Dong, M.Q., Wu, C.C., Venable, J.D., Yates, J.R., 3rd **2007**. ^{15}N metabolic labeling of mammalian tissue with slow protein turnover. J Proteome Res, *6(5)*, 2005-2010.
3. McClatchy, D.B., Liao, L., Park, S.K., Venable, J.D., and Yates, J.R., 3rd **2007**. Quantification of the synaptosomal proteome of the rat cerebellum during post-natal development. Genome Res *17*, 1378-1388.
4. Washburn, M.P., Wolters, D., Yates, J.R., 3rd **2001**. Large-scale analysis of the yeast proteome by multidimensional protein identification technology. Nature Biotechnology *19*, 242-247.
5. Sadygov, R., Cociorva, D., Yates, J.R., 3rd **2004**. Large-scale database searching using tandem mass spectra: looking up the answer in the back of the book. Nature Methods *1*, 195-202.

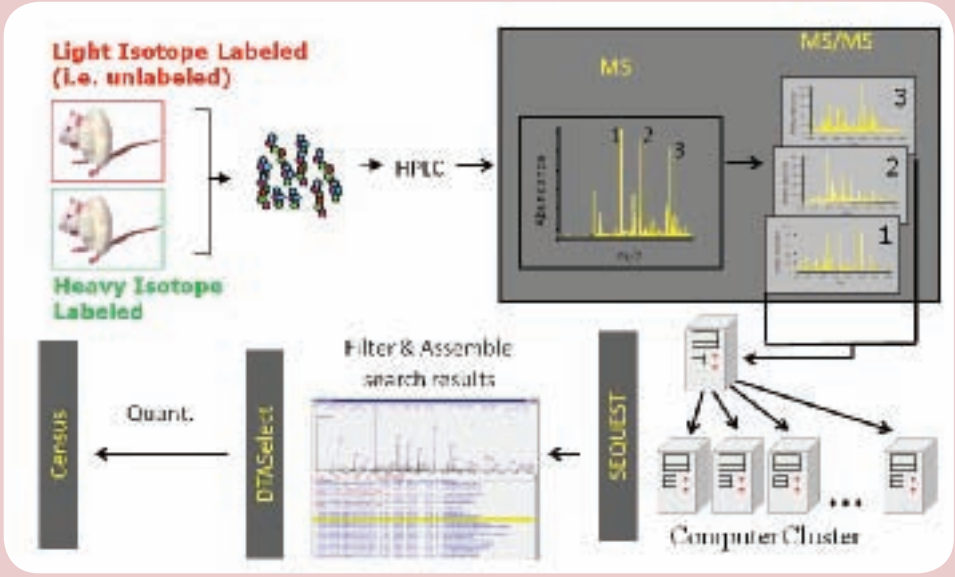


Figure 1: Overview of Relative Quantitation by Stable Isotope Labeling and Mass Spectrometry

New! MouseExpress™ Labeled Mouse Feed

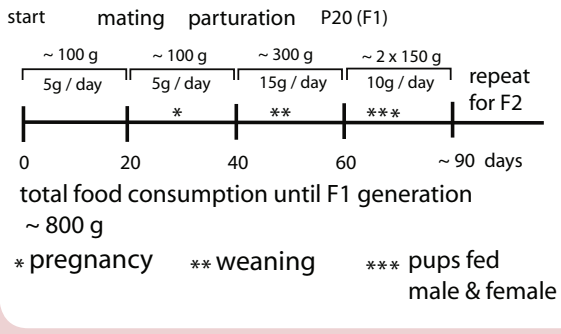
SILAM has also been accomplished utilizing L-Lysine-$^{13}C_6$ (1). CIL is pleased to offer labeled feed for the metabolic incorporation of stable isotope enriched amino acids into mice and rats. **MouseExpress™ L-Lysine ($^{13}C_6$, 99%) mouse feed is prepared using our exclusive 99% enriched L-Lysine-$^{13}C_6$.**

Custom formulations are available in other labeling patterns and amino acid substitutions. Please inquire.

MouseExpress™ L-Lysine ($^{13}C_6$, 99%) Enriched Mouse Feed Labeling Kit

CIL's Mouse Feed Labeling Kit consists of 1 kg L-Lysine-$^{13}C_6$ feed and 1 kg of unlabeled feed. This nutrient mix metabolically labels the entire mouse proteome with L-Lysine-$^{13}C_6$ for use in quantitative global proteomic research using tryptic digests. This diet is unique in that it contains L-Lysine-$^{13}C_6$ at an isotopic enrichment of 99%.

Catalog No.	Description
MLK-LYS-C	**L-Lysine ($^{13}C_6$, 99%) Enriched Mouse Feed Labeling Kit (1kg L-Lysine-$^{13}C_6$ labeled feed/1kg unlabeled feed)**



Mouse feed L-Lysine ($^{13}C_6$, 99%) consumption rate (1).

Spirulina (^{15}N, 98%)

Spirulina (^{15}N, 98%), a unique blue-green algae, in combination with a protein/amino acid-free nutrient mix, provides an efficient feed to metabolically label the entire animal proteome with ^{15}N. A ^{15}N rodent diet can be prepared in your laboratory using ^{15}N Spirulina. Please refer to: McClatchy, D.B. and Yates, J.R., III **2008**. Stable Isotope Labeling of Mammals (SILAM). Cold Spring Harb. Protoc, doi:10.1101/pdb.prot4940

CIL can also provide a prepared feed for your labeling experiments. *Please note a minimum order may be required.*

Catalog No.	Description
NLM-8401	**Spirulina whole cells (lyophilized powder) (^{15}N, 98%)**
ULM-8453	**Spirulina whole cells (lyophilized powder) (unlabeled)**

(^{15}N, 95%) MouseExpress™ Enriched Mouse Tissue
Coming Soon – Uniformly ^{15}N labeled mouse tissue. Please inquire about tissues or organs of interest.

Spirulina (^{13}C, 97%)

Spirulina (^{13}C, 97%), in combination with a nutrient mix, may be used to investigate protein turn-over in a number of organisms including mammals.

Catalog No.	Description
CLM-8400	**Spirulina whole cells (lyophilized powder) (^{13}C, 97%+)**

Reference

1. Krüger, M., Moser, M., Ussar, S., Thievessen, I., Luber, C.A., Forner, F., Schmidt, S., Zanivan, S., Fässler, R., Mann, M. **2008**. SILAC mouse for quantitative proteomics uncovers kindlin-3 as an essential factor for red blood cell function. Cell, *134(2)*, 353-364, S2 Figure F.

New! MouseExpress™ Labeled Mouse Tissue

CIL is pleased to add intact stable isotope enriched mouse tissue to its growing suite of products to assist the mass spectrometry proteomic community. The use of enriched mouse tissue as an internal standard allows for proteomic investigation at the tissue level (1,2) and will accelerate the quantitative proteome comparison across biological samples.

Lysine ($^{13}C_6$, 97%) Enriched Mouse Tissue

MouseExpress™ is freshly frozen, intact mouse tissue that is 97% enriched in L-Lysine-$^{13}C_6$.

MouseExpress™ Lysine ($^{13}C_6$, 97%) enriched mouse tissue is prepared by Silantes (München Germany) for world-wide distribution by CIL (excluding Europe and Japan).

Silantes

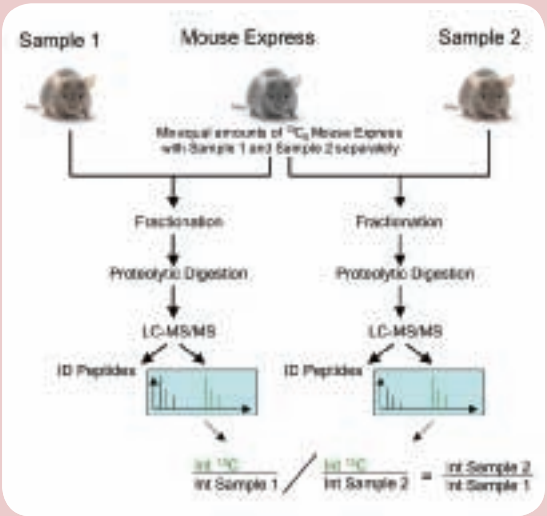
Catalog No.	Description
MT-LYSC6-MBM	**MouseExpress™ Bone Marrow (Male) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-FBM	**MouseExpress™ Bone Marrow (Female) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-MBR	**MouseExpress™ Breast Tissue (Male) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-FBR	**MouseExpress™ Breast Tissue (Female) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-MB	**MouseExpress™ Brain Tissue (Male) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-FB	**MouseExpress™ Brain Tissue (Female) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-MEY	**MouseExpress™ Eye Tissue (Male) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-FEY	**MouseExpress™ Eye Tissue (Female) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-ME	**MouseExpress™ Inner Ear Tissue (Male) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-FE	**MouseExpress™ Inner Ear Tissue (Female) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-MH	**MouseExpress™ Heart Tissue (Male) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-FH	**MouseExpress™ Heart Tissue (Female) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-MK	**MouseExpress™ Kidney Tissue (Male) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-FK	**MouseExpress™ Kidney Tissue (Female) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-ML	**MouseExpress™ Liver Tissue (Male) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-FL	**MouseExpress™ Liver Tissue (Female) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-MLU	**MouseExpress™ Lung Tissue (Male) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-FLU	**MouseExpress™ Lung Tissue (Female) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-MM	**MouseExpress™ Muscle Tissue (Male) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-FM	**MouseExpress™ Muscle Tissue (Female) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-MPL	**MouseExpress™ Plasma (Male) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-FPL	**MouseExpress™ Plasma (Female) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-MSE	**MouseExpress™ Serum (Male) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-FSE	**MouseExpress™ Serum (Female) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-MSK	**MouseExpress™ Skin Tissue (Male) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-FSK	**MouseExpress™ Skin Tissue (Female) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-MSP	**MouseExpress™ Spleen Tissue (Male) L-Lysine ($^{13}C_6$, 97%)**
MT-LYSC6-FSP	**MouseExpress™ Spleen Tissue (Female) L-Lysine ($^{13}C_6$, 97%)**

"The heavy labeled mouse tissue from CIL was extremely useful to validate labeled tissue produced in our own laboratory. We isolated peptides from the CIL tissue and ran our own independent analysis on a mass spectrometer. Based on these analyses we were confident to move forward with our proteomics experiments."

–Dr. Jesse Rinehart
Yale University School of Medicine
Department of Genetics

MouseExpress™ is freshly frozen, intact mouse tissue that is 97% enriched in L-Lysine-$^{13}C_6$.

Various organs and tissues in stock
Strain: C57BL6
Age: Various ages available; please inquire
Isotope enrichment: $^{13}C_6$ in Lys >97%
Form: Intact tissue



Proteomic workflow using MouseExpress™ mouse tissue

References

1. Boettger, T., Beetz, N., Kostin, S., Schneider,J., Krüger, M., Hein, L., Braun, T. **2009.** Acquisition of the contractile phenotype by murine arterial smooth muscle cells depends on the Mir143/145 gene cluster. J Clin Invest, *119(9)*, 2634-2647.
2. McClatchy, D.B., Dong, M.Q., Wu, C.C., Venable, J.D., Yates, J.R., 3rd **2007**. ^{15}N metabolic labeling of mammalian tissue with slow protein turnover. J Proteome Res, *6(5)*, 2005-2010.

Amino Acids and Additional Metabolic Labeling Products

New! 99% Enriched Amino Acids

Higher enrichments provide improved accuracy in quantitative MS-based proteomic applications. These materials represent the highest isotopically enriched amino acids that are commercially available.

Catalog No.	Description
CLM-2247-H	L-Lysine•2HCl (U-$^{13}C_6$, 99%)
CNLM-291-H	L-Lysine•2HCl (U-$^{13}C_6$, 99%; $^{15}N_2$, 99%)
CLM-2265-H	L-Arginine•HCl (U-$^{13}C_6$, 99%)
CNLM-539-H	L-Arginine•HCl (U-$^{13}C_6$, 99%; $^{15}N_4$, 99%)
CLM-2262-H	L-Leucine (U-$^{13}C_6$, 99%)
CNLM-281-H	L-Leucine (U-$^{13}C_6$, 99%; ^{15}N, 99%)
CLM-2248-H	L-Isoleucine (U-$^{13}C_6$, 99%)
CNLM-561-H	L-Isoleucine (U-$^{13}C_6$, 99%; ^{15}N, 99%)

> "Using highly enriched materials decreases the amount of unlabeled analog introduced into the mass spectrometer. As a result, using 99% enriched amino acids will increase the accuracy and useful dynamic range for MS-based quantitative proteomic methods compared to using amino acids with lower enrichments."
>
> *– Michael Burgess*
> *Senior Biochemist*
> *Broad Institute*

Primary SI Labeled Amino Acids

Catalog No.	Description
CLM-2265	L-Arginine•HCl (U-$^{13}C_6$, 97-99%)
NLM-395	L-Arginine•HCl (guanido-$^{15}N_2$, 98%+)
NLM-396	L-Arginine•HCl (U-$^{15}N_4$, 98%)
CNLM-539	L-Arginine•HCl (U-$^{13}C_6$, 97-99%; U-$^{15}N_4$, 97-99%)
CDNLM-6801	L-Arginine•HCl (U-$^{13}C_6$, 97-99%; U-D_7, 97-99%; U-$^{15}N_4$, 97-99%)
CLM-2248	L-Isoleucine (U-$^{13}C_6$, 97-99%)
CNLM-561	L-Isoleucine (U-$^{13}C_6$, 97-99%; ^{15}N, 97-99%)
CLM-2262	L-Leucine (U-$^{13}C_6$, 97-99%)
DLM-1259	L-Leucine (5,5,5-D_3, 98%)
CNLM-281	L-Leucine (U-$^{13}C_6$, 97-99%; ^{15}N, 97-99%)
CLM-2247	L-Lysine•2HCl (U-$^{13}C_6$, 97-99%)
DLM-2640	L-Lysine•2HCl (4,4,5,5-D_4, 96-98%)
NLM-143	L-Lysine•2HCl (α-^{15}N, 95-99%)
NLM-631	L-Lysine•2HCl (ε-^{15}N, 98%+)
NLM-1554	L-Lysine•2HCl ($^{15}N_2$, 96%+)
CNLM-291	L-Lysine•2HCl (U-$^{13}C_6$, 97-99%; U-$^{15}N_2$, 97-99%)
CDNLM-6810	L-Lysine•2HCl (U-$^{13}C_6$, 97-99%; U-D_9, 97-99%; U-$^{15}N_2$, 97-99%)
DLM-431	L-Methionine (methyl-D_3, 98%)
CDLM-760	L-Methionine (1-^{13}C, 99%; methyl-D_3, 98%)
CNLM-759	L-Methionine (U-$^{13}C_5$, 97-99%; ^{15}N, 97-99%)
CLM-2250	L-Phenylalanine (U-$^{13}C_9$, 97-99%)
CNLM-575	L-Phenylalanine (U-$^{13}C_9$, 97-99%; ^{15}N, 97-99%)
CLM-2261	L-Threonine (U-$^{13}C_4$, 97-99%)
CNLM-587	L-Threonine (U-$^{13}C_4$, 97-99%; ^{15}N, 97-99%)
CLM-1542	L-Tyrosine (ring-$^{13}C_6$, 99%)
CLM-2263	L-Tyrosine (U-$^{13}C_9$, 97-99%)
CNLM-439	L-Tyrosine (U-$^{13}C_9$, 97-99%; ^{15}N, 97-99%)
CLM-2249	L-Valine (U-$^{13}C_5$, 97-99%)
CNLM-442	L-Valine (U-$^{13}C_5$, 97-99%; ^{15}N, 97-99%)

Primary Natural Abundance Amino Acids

Catalog No.	Description
ULM-8347	L-Arginine•HCl
ULM-8766	L-Lysine•2HCl
ULM-8333	L-Proline

Additional Metabolic Labeling Products

Catalog No.	Description
NLM-467	Ammonium chloride (^{15}N, 99%)
DNLM-8739	Ammonium chloride (D_4, 98%; ^{15}N, 98%)
NLM-1320	Ammonium hydroxide (^{15}N, 98%)(3.3N IN H_2O)
NLM-713	Ammonium sulfate ($^{15}N_2$, 99%)
DNLM-3322	Ammonium sulfate ($^{15}N_2$, 99%; D_8, 98%)
NLM-765	Potassium nitrate (^{15}N, 99%)
DLM-4	Deuterium oxide (D, 99.9%)
DLM-4-99.8	Deuterium oxide (D, 99.8%)
DLM-4-99	Deuterium oxide (D, 99%)
CLM-4819	D-Glucose (U-$^{12}C_6$, 99.9%)
CLM-1396	D-Glucose (U-$^{13}C_6$, 99%)
DLM-2062	D-Glucose (1,2,3,4,5,6,6-D_7, 98%)
CDLM-3813	D-Glucose (U-$^{13}C_6$, 99%; 1,2,3,4,5,6,6-D_7, 97-98%)

Enriched Cell Growth Media

The study of protein function often require proteins expressed in isotopically labeled media. CIL has developed cell growth media products for protein expression at levels necessary for MS proteomics research and NMR structural studies. Whether your protein of interest is expressed from bacterial cells in minimal or rich media, yeast cells, the Sf9/ baculovirus expression system or mammalian cell expression systems, CIL offers a full range of products to give you a choice of labeling patterns. A complete description of our cell growth media is available in our **Stable Isotope Labeled Media Products** brochure.

Rich Bacterial Cell Growth Media

Celtone® Powder (*E. coli* and Other Bacteria)

CIL'S most flexible media, Celtone Base Powder, is a mixture of amino acids, peptides, vitamins and other essential nutrients, which provides a "rich" environment for excellent bacterial cell growth and high protein expression. The powder is easy to use and store and has the longest shelf life of any fully-rich bacterial growth medium.

Celtone® Complete (*E. coli* and Other Bacteria)

Celtone Complete Medium is a "rich" bacterial cell growth medium derived from an algal source with a growth rate comparable to LB, allowing for inoculation and induction within one working day. Celtone Complete Medium is formulated as a ready-to-use medium.

BioExpress®1000 (*E. coli* and Other Bacteria)

CIL's all-time classic bacterial cell growth medium. This media is comprised of a complex mixture of glucose, amino acids, peptides, vitamins, minerals and cofactors. Prepared from algal cell hydrolysates and processed using a proprietary procedure, BioExpress®1000 yields excellent growth and expression characteristics for a number of different bacterial systems.

Silantes® *E. coli*-OD_2

Silantes *E. coli*-OD_2 is made from bacterial hydrolysate and contains primarily amino acids, some low MW oligopeptides and almost no carbohydrates. Silantes OD-Media have the same characteristics as conventional LB media.

Minimal Media for Bacterial Cell Growth

Spectra 9 (*E. coli* and Other Bacteria)

Spectra 9 is a cost-effective medium for *E. coli* bacterial growth and protein expression. It is comprised of labeled salts and labeled carbohydrates, and is supplemented with Celtone® Base Powder (1g powder per liter Spectra 9) which contains amino acids, vitamins, peptides and other essential nutrients.

Additional Products for Bacterial Minimal Media

Labeled glucose, ammonium salts, glycerol and deuterium oxide are available.

Insect Cell Growth Media

BioExpress®2000 for Insect Expression Systems

The Baculovirus Expression Vector System (BEVS) has grown to become the most versatile and widely used eukaryotic vector system employed for the expression of recombinant proteins in cultured insect cells. Amino acid selective labeling is possible with BioExpress®2000 because the amino acid content is chemically defined.

Mammalian Cell Growth Media

BioExpress®6000 for Mammalian Expression Systems

The expression of recombinant mammalian proteins in mammalian cell lines show the greatest promise to produce correctly folded proteins with the greatest number of post-translational modifications. This media should work well with cell lines grown in DMEM. Amino acid selective labeling is possible with BioExpress®6000 because the amino acid content is chemically defined.

Yeast Cell Growth Media

Silantes® Yeast-OD_2

Yeast is used for the expression of eukaryotic proteins, since this host facilitates high protein expression and many post-translational protein modifications characteristic for mammalian cells.

Cell Free *(in vitro)*

If a protein cannot be expressed or folded correctly using an *in vivo* expression system, the use of *in vitro* protein expression systems may be an option. The *in vitro* systems can be used to express toxic proteins and the open system allows for selective labeling schemes as well as the addition of exogenous molecules (e.g. detergents) to assist in obtaining soluble functional protein.

The CellFree Sciences (CFS) WEPRO Expression Kit utilizes a wheat germ extract and includes a formulation of CIL uniformly labeled amino acids in their SUB-AMIX component of the kit.

Exclusively distributed by CIL in North America and Europe.

Qiagen EasyXpress® systems utilize *E. coli* extract. The EasyXpress NMR Protein Synthesis and Uniform Labeling Kit includes a formulation of CIL uniformly labeled amino acids.

Exclusively distributed by CIL world-wide.

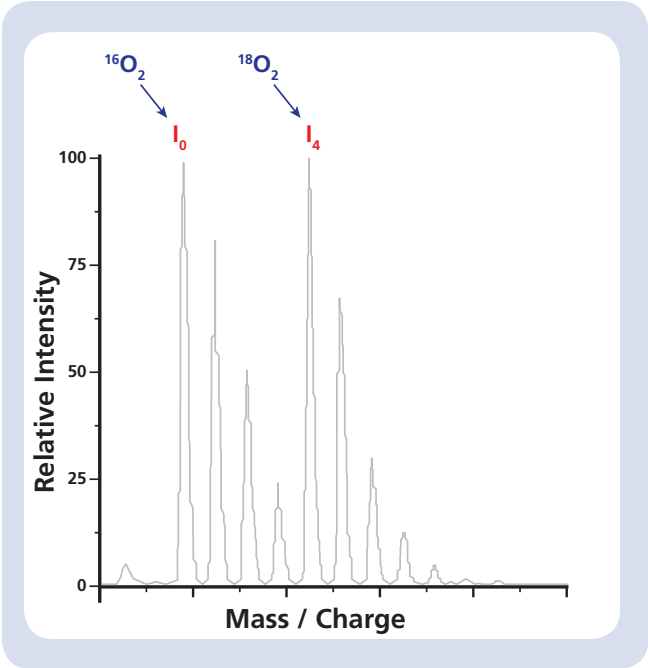
^{18}O Labeling

$^{18}O_2$-labeling is the Linux of isotope labeling methods. Any laboratory can buy $H_2{}^{18}O$ and adapt the method to its own applications. It offers a universal strategy for uniform labeling of all peptides from any kind of protein, including modified proteins (1). It is used to label clinical samples with unrivaled sensitivity (2,3). The only byproduct is water, and the immobilized catalytic enzyme can be removed mechanically. Labeling with $^{18}O_2$ is limited to binary comparisons or series thereof, and it requires a workflow with minimal manipulation of proteins since the light and heavy samples are combined at the peptide level.

Two atoms of ^{18}O are introduced into the carboxylic acid group of every proteolytic peptide in a protein pool that has been catalyzed by members of the serine protease family, which includes trypsin, Glu-C protease, Lys-C protease and chymotrypsin. In the binding site of each protease, the residue of choice is covalently bound in a tetrahedral intermediate, which is then disrupted by nucleophilic attack by a water molecule, cleaving the protein. The C-terminal residue in each peptide product is re-bound by the protease, e.g., Arginine and Lysine in the case of trypsin, and released by hyrolysis. If the peptide products are incubated with the catalytic enzyme in $H_2{}^{18}O$, the level of ^{18}O in the peptides will eventually equilibrate with the level of ^{18}O in the solvent, preferably > 95%. Peptide binding by the protease offers the advantage that cleavage of the protein can be optimized and carried out separately from labeling the peptide (4).

Each heavy peptide weighs 4 Da more than its $^{16}O_2$ light analog. After labeling, the mixtures of heavy and light peptides are mixed, and isotope ratios of peptide pairs are determined by LC-MS. Concurrent MSMS measurements and appropriate computer algorithms can provide peptide identification along with quantitation.

– Dr. Catherine Fenselau
University of Maryland



Enzymatic Labeling Products

The incorporation of two ^{18}O atoms into each C-terminus of peptides derived from proteolytic digestion of biological samples has emerged as one of the leading global labeling strategies used in comparative quantitative proteomics. The success of the technique is due in part to the relative low cost of ^{18}O water, the resulting +4 dalton mass increase in molecular weight for the "heavy" peptide, and co-elution of $^{18}O/^{16}O$ peptide pairs from reverse-phase HPLC.

CIL is pleased to announce the availability of Water (^{18}O, 99%). This highly enriched material allows for the most complete labeling of peptides for proteomic applications.

Water (^{18}O)

Catalog No.	Description
OLM-240-99	**Water (^{18}O, 99%)**

Water (^{17}O)

Catalog No.	Description
OLM-782-90	**Water (^{17}O, 90%)**
OLM-782-70	**Water (^{17}O, 70%)**

References

1. Fenselau, C., Yao, Z. **2009**.$^{18}O_2$-Labeling in quantitative proteomic strategies: a status report. J Proteome Res, *8(5)*, 2140-2143.
2. Zang, L., Palmer Toy, D., Hancock, W.S., Sgroi, D.C., Karger, B.L. **2004**. Proteomic analysis of ductal carcinoma of the breast using laser capture microdissection, LC-MS and $^{16}O/^{18}O$ isotopic labeling. J Proteome Res, *3(3)*, 604-612.
3. Bantscheff, M., Dumpelfeld, B., Kuster, B. **2004**. Femtomol sensitivity post-digest ^{18}O labeling for relative quantification of differential protein complex composition. Rapid Commun Mass Spectrom, *18(8)*, 869-876.
4. Yao, X., Afonso, C., Fenselau, C. **2003**. Dissection of proteolytic ^{18}O labeling: endoprotease-catalyzed ^{16}O-to-^{18}O exchange of truncated peptide substrates. J Proteome Res, *2(2)*, 147-152.

Synthetic Peptides As Internal Standards

The addition of synthetic internal standards has been used for nearly 40 years for quantitation with mass spectrometry (1). It is particularly useful with LC-ES-MS and MALDI-MS for proteomic analyses. In the most common workflow for proteomics, peptides are selected based on uniqueness, stability, chromatographic behavior and sensitivity to ionization techniques to serve as surrogate markers for proteins of interest. Internal standards are added to allow these peptides and the proteins they represent to be quantified. The best internal standards are peptides that have identical sequences as the biomarker peptides, and carry stable isotopic labels (2). The isotopes change the mass, but not the chemical behavior. Isotope ratios of spiked peptides and peptides obtained from protein biomarkers are measured by mass spectrometry and tandem mass spectrometry to provide absolute quantitation of the endogenous protein (3,4). The use of internal standards allows multiple peptides (and thus multiple proteins) to be quantified in a single sample, and facile quantitation of a particular peptide in multiple samples, e.g., at multiple time points. The approach is applicable to quantitation of proteins in tissue samples as well as proteins in solution. Peptides with homologous sequences and different masses (and no isotope labels) can also be used as internal standards, supported by standard curves. Isotope-labeled proteins provide even better internal standards because they undergo fractionation and digestion along with the biomarker proteins and provide correction for losses that occur before peptides are produced. Such proteins may be provided from normal or recombinant cells grown in labeled media.

– Dr. Catherine Fenselau
University of Maryland

“The commercial availability of stable-isotope labeled amino acids with very high isotopic purity has revolutionized quantitative proteomics. From their use in metabolic labeling of cells and rodents for differential discovery proteomics, to their use in synthetic peptides as internal standards for targeted analysis of proteins, isotopically-labeled amino acids make it possible to measure, with very high precision, changes in the levels of peptides and the proteins they are derived from in highly complex samples such as cell lysates, tissue and plasma. Cambridge Isotope Labs has been and continues to be a leader in the commercial production of labeled amino acids and other labeled compounds ”.

– Dr. Steven A. Carr
Broad Institute of MIT and Harvard

Custom Labeled Peptides

Stable-isotope labeled peptides are used in biomarker discovery and validation as well as in drug and metabolite monitoring, peptide signaling experiments, metabolomics and pharmacokinetics. CIL is pleased to supply highly enriched and pure amino acids to the world’s leading peptide manufacturers.

As a value-added service, we are also able to provide a quotation on your custom labeled peptide requirements.

References

1. Fenselau, C. **1977**. The mass spectrometer as a gas chromatograph detector. Anal Chem, *49(6)*, 563A-570A.
2. Desiderio, D.M., Kai, M. **1983**. Preparation of stable isotope-incorporated peptide internal standards for field desorption mass spectrometry quantification of peptides in biologic tissue. Biomed Mass Spectrom, *10(8)*, 471-479.
3. Gerber, S.A., Rush, J., Stemman, O., Kirschner, M.W., Gygi, S.P. **2003**. Absolute quantification of proteins and phosphoproteins from cell lysates by tandem MS. Proc Natl Acad Sci USA, *100(12)*, 6940-6945.
4. Anderson, L., Hunter, C.L. **2006**. Quantitative mass spectrometric multiple reaction monitoring assays for major plasma proteins. Mol Cell Proteomics, *5(4)*, 573-588.

Protected Amino Acids

Catalog No.	Description
CNLM-4355	L-Alanine-N-FMOC (U-$^{13}C_3$, 97-99%; ^{15}N, 97-99%)
CDNLM-7852	L-Alanine-N-FMOC (U-$^{13}C_3$, 97-99%; U-D_4, 97-99%; ^{15}N, 97-99%)
DLM-8168	L-Alanine-N-FMOC (2,3,3,3-D_4, 98%)
CLM-3589	L-Alanine-N-*t*-BOC (U-$^{13}C_3$, 97-99%)
CNLM-2394	L-Alanine-N-*t*-BOC (U-$^{13}C_3$, 97-99%; ^{15}N, 97-99%)
New! CLM-8475-H	L-Arginine-N-FMOC, Pbf (U-$^{13}C_6$, 99%) (Contains Ethyl Acetate)
New! CNLM-8474-H	L-Arginine-N-FMOC, Pbf (U-$^{13}C_6$, 99%; U-$^{15}N_4$, 99%) (Contains Ethyl Acetate)
CLM-7792	L-Arginine-N-FMOC, Pmc (U-$^{13}C_6$, 97-99%) (CP ≥ 94%)
NLM-1264	L-Arginine-N-FMOC, Pmc (U-$^{15}N_4$, 98%) (CP ≥ 94%)
CNLM-4226	L-Arginine-N-FMOC, Pmc (U-$^{13}C_6$, 97-99%; U-$^{15}N_4$, 97-99%) (CP ≥ 94%)
CNLM-4354	L-Asparagine-N-FMOC (U-$^{13}C_4$, 97-99%; U-$^{15}N_2$, 97-99%)
CNLM-6193	L-Asparagine-N-FMOC, N-β-Trityl (U-$^{13}C_4$, 97-99%; U-$^{15}N_2$, 97-99%)
CNLM-4788	L-Aspartic Acid-N-FMOC (U-$^{13}C_4$, 97-99%; ^{15}N, 97-99%)
CNLM-4789	L-Aspartic Acid-N-FMOC, α-O-*t*-Butyl Ester (U-$^{13}C_4$, 97-99%;^{15}N, 97-99%)
CNLM-4752	L-Aspartic Acid-N-FMOC, β-O-*t*-Butyl Ester (U-$^{13}C_4$, 97-99%; ^{15}N, 97-99%)
CNLM-2392	L-Aspartic Acid-N-*t*-BOC, β-Benzyl Ester (U-$^{13}C_4$, 97-99%; ^{15}N, 97-99%)
CNLM-7579	L-Cysteine, N-Acetyl (cysteine-$^{13}C_3$, 97-99%; ^{15}N, 97-99%) (CP ≥ 95%)
CNLM-7112	L-Cysteine, S-Trityl (U-$^{13}C_3$, 97-99%; ^{15}N, 97-99%)
CNLM-4722	L-Cysteine-N-FMOC, S-Trityl (U-$^{13}C_3$, 97-99%; ^{15}N, 97-99%)
CLM-6664	L-Glutamic Acid, N-Acetyl (glutamate-$^{13}C_5$, 97-99%)
CNLM-4753	L-Glutamic Acid-N-FMOC, γ-*t*-Butyl Ester (U-$^{13}C_5$, 97-99%; ^{15}N, 97-99%) (CP ≥ 96%)
CNLM-4356	L-Glutamine-N-FMOC (U-$^{13}C_5$, 97-99%; U-$^{15}N_2$, 97-99%)
CNLM-7252	L-Glutamine-N-FMOC, N-γ-Trityl (U-$^{13}C_5$, 97-99%; U-$^{15}N_2$, 97-99%)
CNLM-4524	Glycine, N-Acetyl (U-$^{13}C_2$, 97-99%; ^{15}N, 97-99%
CNLM-4357	Glycine-N-FMOC (U-$^{13}C_2$, 97-99%; ^{15}N, 97-99%)
CDNLM-7853	Glycine-N-FMOC (U-$^{13}C_2$, 97-99%; 2,2-D_2, 97-99%; ^{15}N, 97-99%)
CNLM-2412	Glycine-N-*t*-BOC (U-$^{13}C_2$, 97-99%; ^{15}N, 97-99%)

Catalog No.	Description
NLM-8010	L-Histidine-N-FMOC, N-IM-Trityl ($^{15}N_3$, 98%)
CLM-7794	L-Isoleucine-N-FMOC (U-$^{13}C_6$, 97-99%)
CNLM-4346	L-Isoleucine-N-FMOC (U-$^{13}C_6$, 97-99%; ^{15}N, 97-99%)
CLM-3683	L-Leucine-N-FMOC (U-$^{13}C_6$, 97-99%)
DLM-7575	L-Leucine-N-FMOC (D_{10}, 98%)
CNLM-4345	L-Leucine-N-FMOC (U-$^{13}C_6$, 97-99%;^{15}N, 97-99%)
CDNLM-7854	L-Leucine-N-FMOC (U-$^{13}C_6$, 97-99%; U-D_{10}, 97-99%; ^{15}N, 97-99%)
DLM-3650	L-Leucine-N-*t*-BOC•H_2O (D_{10}, 98%)
CNLM-2396	L-Leucine-N-*t*-BOC•H_2O (U-$^{13}C_6$, 97-99%; ^{15}N, 97-99%)
New! CLM-7865-H	L-Lysine-α-N-FMOC, ε-N-*t*-BOC (U-$^{13}C_6$, 99%)
New! CNLM-4754-H	L-Lysine-α-N-FMOC, ε-N-*t*-BOC (U-$^{13}C_6$, 99%; U-$^{15}N_2$, 99%)
CNLM-4358	L-Methionine-N-FMOC (U-$^{13}C_5$, 97-99%; ^{15}N, 97-99%)
CLM-4248	L-Phenylalanine, Methyl Ester•HCl (U-$^{13}C_{10}$, 97-99%)
CLM-3684	L-Phenylalanine-N-FMOC (ring-$^{13}C_6$, 99%)
CNLM-4362	L-Phenylalanine-N-FMOC (U-$^{13}C_9$, 97-99%; ^{15}N, 97-99%)
DLM-8752	L-Phenylalanine-N-FMOC (D_8, 98%)
CLM-2061	L-Phenylalanine-N-*t*-BOC (ring-$^{13}C_6$, 99%)
CLM-7859	L-Phenylalanine-N-*t*-BOC (U-$^{13}C_9$, 97-99%)
CNLM-2393	L-Phenylalanine-N-*t*-BOC (U-$^{13}C_9$, 97-99%; ^{15}N, 97-99%)
DLM-2157	L-Phenylalanine-N-*t*-BOC (ring-D_5,98%)
CNLM-4347	L-Proline-N-FMOC (U-$^{13}C_5$, 97-99%; ^{15}N, 97-99%)
CNLM-8403	L-Serine-N-FMOC (U-$^{13}C_3$, 97-99%; ^{15}N, 97-99%)
CNLM-4755	L-Serine-N-FMOC, O-*t*-Butyl Ether (U-$^{13}C_3$, 97-99%; ^{15}N, 97-99%) 3% D-isomer
CNLM-7615	L-Threonine-N-FMOC, O-*t*-Butyl Ether (U-$^{13}C_4$, 97-99%; ^{15}N, 97-99%)
DLM-6113	L-Tryptophan-N-FMOC (Indole-D_5, 98%)
CNLM-6077	L-Tryptophan-N-FMOC (U-$^{13}C_{11}$, 97-99%; U-$^{15}N_2$, 97-99%)
CNLM-4349	L-Tyrosine-N-FMOC, O-*t*-Butyl Ether (U-$^{13}C_9$, 97-99%; ^{15}N, 97-99%)
CLM-2092	L-Tyrosine-N-*t*-BOC, O-Bz Ether (ring-$^{13}C_6$, 99%)
CLM-7793	L-Valine-N-FMOC (U-$^{13}C_5$, 97-99%)
DLM-7784	L-Valine-N-FMOC (D_8, 98%)
CNLM-4348	L-Valine-N-FMOC (U-$^{13}C_5$, 97-99%; ^{15}N, 97-99%)
DLM-3651	L-Valine-N-*t*-BOC (D_8, 98%)
CNLM-2395	L-Valine-N-*t*-BOC (U-$^{13}C_5$, 97-99%; ^{15}N, 97-99%)

99% Enriched
Please inquire about additional protected amino acids meeting this specification.

A complete listing of CIL's protected amino acids is available in our Stable Isotope Labeled Protected Amino Acids brochure at isotope.com.

Tagging Reagents and Related Products

"We have come to depend on CIL to furnish us with high quality reagents during the past few years as our laboratory became interested in the synthesis of a series of isotopically labeled coding agents for quantification in both proteomics and metabolomics. CIL was both knowledgeable and helpful, being willing to listen to our problems and going to their technical staff for solutions. Relationships like this are infrequent today and extremely valuable when you need answers quickly."

– Dr. Fred E. Regnier
J.H. Law Distinguished Professor
Department of Chemistry, Purdue University

Catalog No.	Description
CLM-173	**Acetaldehyde (1,2-$^{13}C_2$, 99%)**
DLM-112	**Acetaldehyde (D_4, 99%)**
CLM-1161	**Acetic anhydride (1,1',2,2'-$^{13}C_4$, 99%)**
DLM-1162	**Acetic anhydride (D_6, 98%)**
DLM-9	**Acetone (D_6, 99.9%)**
DLM-247	**Acetyl chloride (D_3, 98%)**
CDLM-6208	**Acetyl chloride ($^{13}C_2$, 99%; D_3, 98%)**
CLM-813	**Acrylamide (1,2,3-$^{13}C_3$, 99%)**
DLM-821	**Acrylamide (2,3,3-D_3, 98%)**
OLM-7858	**Adenosine 5'-triphosphate, sodium salt (γ-$^{18}O_4$, 97%)**
CLM-714	**Aniline ($^{13}C_6$, 99%)**
CLM-182	**Benzene ($^{13}C_6$, 99%)**
CLM-1813	**Benzoic acid (ring-$^{13}C_6$, 99%)**
CLM-3010	**Benzoyl chloride (carbonyl-^{13}C, 99%)**
DLM-595	**Benzoyl chloride (D_5, 99%)**
CLM-1339	**Bromoacetic acid (1,2-$^{13}C_2$, 99%)**
CLM-871	**Bromobenzene ($^{13}C_6$, 99%)**
DLM-103	**2-Bromoethanol (1,1,2,2-D_4, 98%) (CP ≥ 95%)**
CLM-1829	**Chlorobenzene ($^{13}C_6$, 99%)**
DLM-341	**1,4-Dibromobenzene (D_4, 98%)**
DLM-267	**Dimethylamine (D_6, 99%) (gas)**
CLM-266	**Dimethyl sulfate ($^{13}C_2$, 99%)**
DLM-196	**Dimethyl sulfate (D_6, 98%)**
DLM-2622	**DL-1,4-Dithiothreitol (D_{10}, 98%)**
DLM-6785	**1,2-Ethanedithiol (1,1,2,2-D_4, 98%)**
DLM-552	**Ethanolamine (D_4, 98%)**
CLM-3297	**Ethyl acetoacetate (1,2,3,4-$^{13}C_4$, 99%)**
DLM-271	**Ethylene oxide (D_4, 98%) (stabilized with 0.1% hydroquinone)**
DLM-6711	**N-Ethylmaleimide (ethyl-D_5, 98%)**

Catalog No.	Description
CLM-806	**Formaldehyde (^{13}C, 99%) (~20% w/w in H_2O)**
DLM-805	**Formaldehyde (D_2, 98%) (~20% w/w in D_2O)**
CDLM-4599	**Formaldehyde (^{13}C, 99%; D_2, 98%) (20% w/w in D_2O)**
CNLM-7333	**Guanidine·HBr (^{13}C, 99%: $^{15}N_3$, 98%)**
CNLM-7138	**Guanidine:HCl (^{13}C, 99%; $^{15}N_3$, 98%)**
DLM-1229	**Glycerol (1,1,2,2,3,3-D_5, 99%)**
DLM-7249	**Iodoacetamide (D_4, 98%)**
CLM-3264	**Iodoacetic acid (2-^{13}C, 99%)**
DLM-1136	**Isopropanol (dimethyl-D_6, 98%)**
DLM-598	**Methanol (D_3, 99.5%)**
CDLM-688	**Methanol (^{13}C, 99%; D_4, 99%)**
CDLM-8241	**Methylamine·HCl (^{13}C, 99%; D_3, 98%)**
CDNLM-8182	**Methylamine·HCl (^{13}C, 99%; methyl-D_3, 98%; ^{15}N, 98%)**
CNLM-6088	**O-Methylisourea hydrogen chloride (isourea-^{13}C, 99%; $^{15}N_2$, 98%) (CP ≥ 95%)**
DLM-2872	**Nicotinic acid, ethyl ester (2,4,5,6-D_4, 98%)**
CLM-675	**Nitrobenzene ($^{13}C_6$, 99%)**
CLM-6586	**2-Nitrobenzenesulfenyl chloride ($^{13}C_6$, 99%)**
CLM-216	**Phenol ($^{13}C_6$, 99%)**
DLM-7731	**Phenyl isocyanate (phenyl-D_5, 98%)**
OLM-1057	**Phosphoric acid ($^{18}O_4$, 96%) 80-85% in water-^{18}O**
OLM-7493	**Potassium dihydrogen phosphate ($^{18}O_4$, 97%)**
OLM-7523	**Potassium phosphate (^{18}O, 97%)**
DLM-599	**Propionic acid (D_6, 98%)**
DLM-3305	**Propionic anhydride (D_{10}, 98%)**
DLM-1067	**1,2-Propylene oxide (D_6, 98%) (stabilized with hydroquinone)**
DLM-3126	**Sodium acetate (D_3, 99%)**
CDLM-611	**Sodium acetate (1-^{13}C, 99%; D_3, 98%)**
CDLM-1240	**Sodium acetate (2-^{13}C, 99%; D_3, 98%)**
CDLM-3457	**Sodium acetate (1,2-$^{13}C_2$, 99%; D_3, 98%)**
DLM-7364	**Sodium cyanoborodeuteride (D_3, 98%)**
CLM-2473	**Succinic anhydride (1,2,3,4-$^{13}C_4$, 99%)**
DLM-833	**Succinic anhydride (D_4, 98%)**
CLM-1571	**Succinic acid ($^{13}C_4$, 99%)**
CDLM-7754	**Succinic acid ($^{13}C_4$, 99%; 2,2,3,3-D_4, 98%)**
DLM-1176	**Toluene (ring-D_5, 98%)**
CLM-311	**Urea (research grade) (^{13}C, 99%)**
NLM-233	**Urea ($^{15}N_2$, 98%)**

For our international customers

To request a quotation or place an order,
please contact CIL International Sales at
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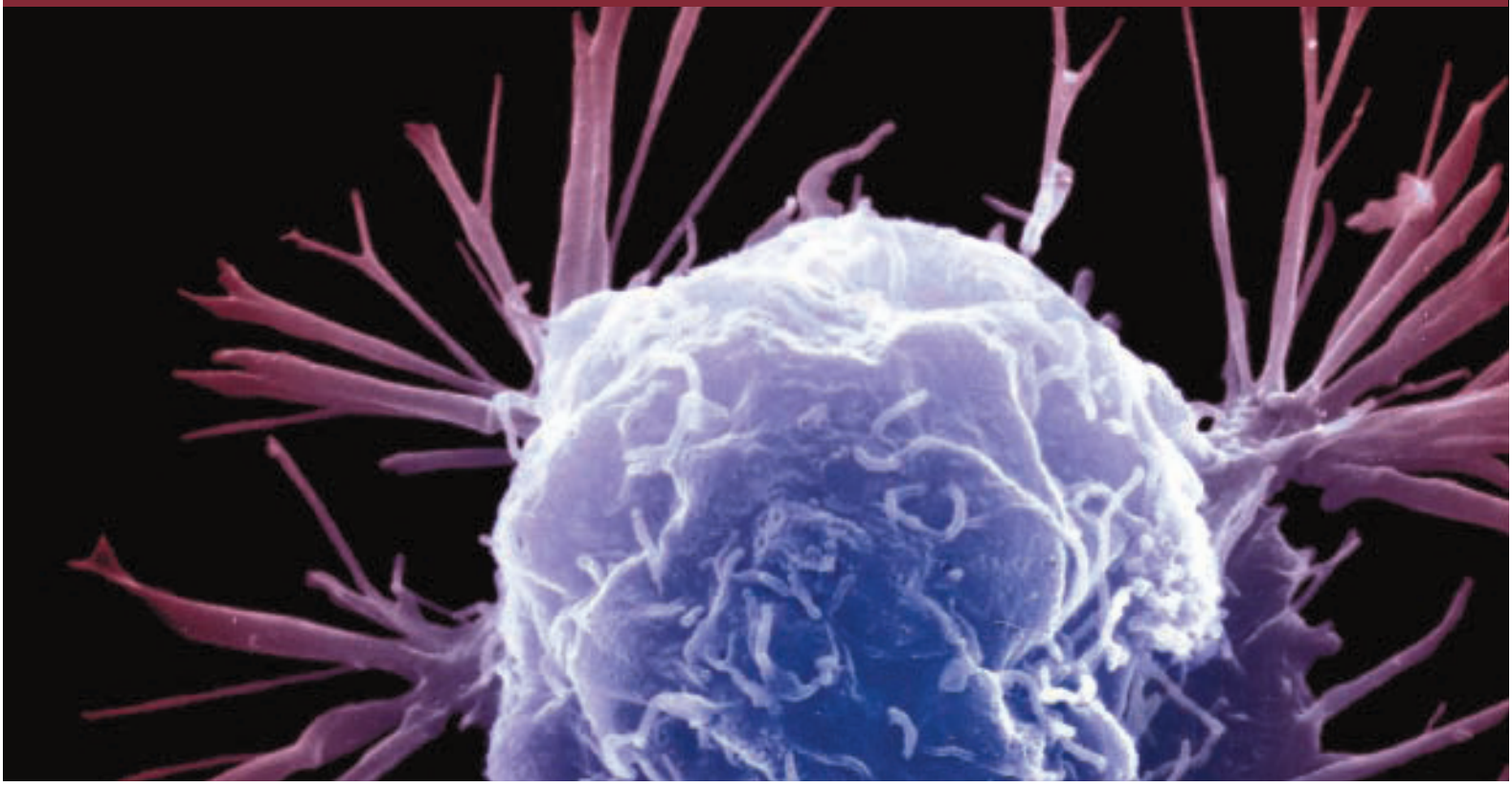
CIL has an established network of 27 independent international distributors. Most of our distributors have worked with CIL for more than ten years. CIL's distributor listing is on our website, isotope.com.



Also Available

Product literature is available for download at isotope.com or contact CIL's Customer Service group.

Stable Isotope Labeled Media Products

- Bacteria Cell Growth
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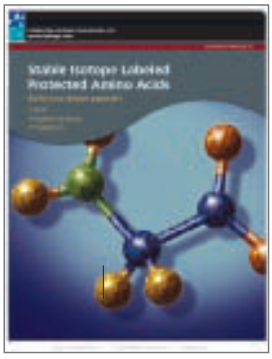
- Mammalian Cell Growth
- Yeast Cell Growth



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