When Balance is Everything, You Have to Stay a Step Ahead

Feel balanced. Feel better.

GLYTACTIN

CAMBROOKE THERAPEUTICS™

Many steps ago, our passion for achieving metabolic balance led us to Glytactin (GMP)

Our Philosophy Drives Our Innovation

Focus on Balance to Feel Better

Cambrooke Pioneered a Paradigm Shift in Medical Formula

Amino Acids → **Whole Protein GMP**

1970s

Phenyl-Free

First PKU Formula -
Amino Acid-Based Medical Food

2010

BetterMilk

First Commercial
GMP Formula for PKU

New formats and calorie options

Restore Complete Swirl

2012

2014

Glytactin RTD

Convenient Consumer Friendly Packaging

BetterMilk Lite

2015

2017

BUILD Restore Lite - Powder

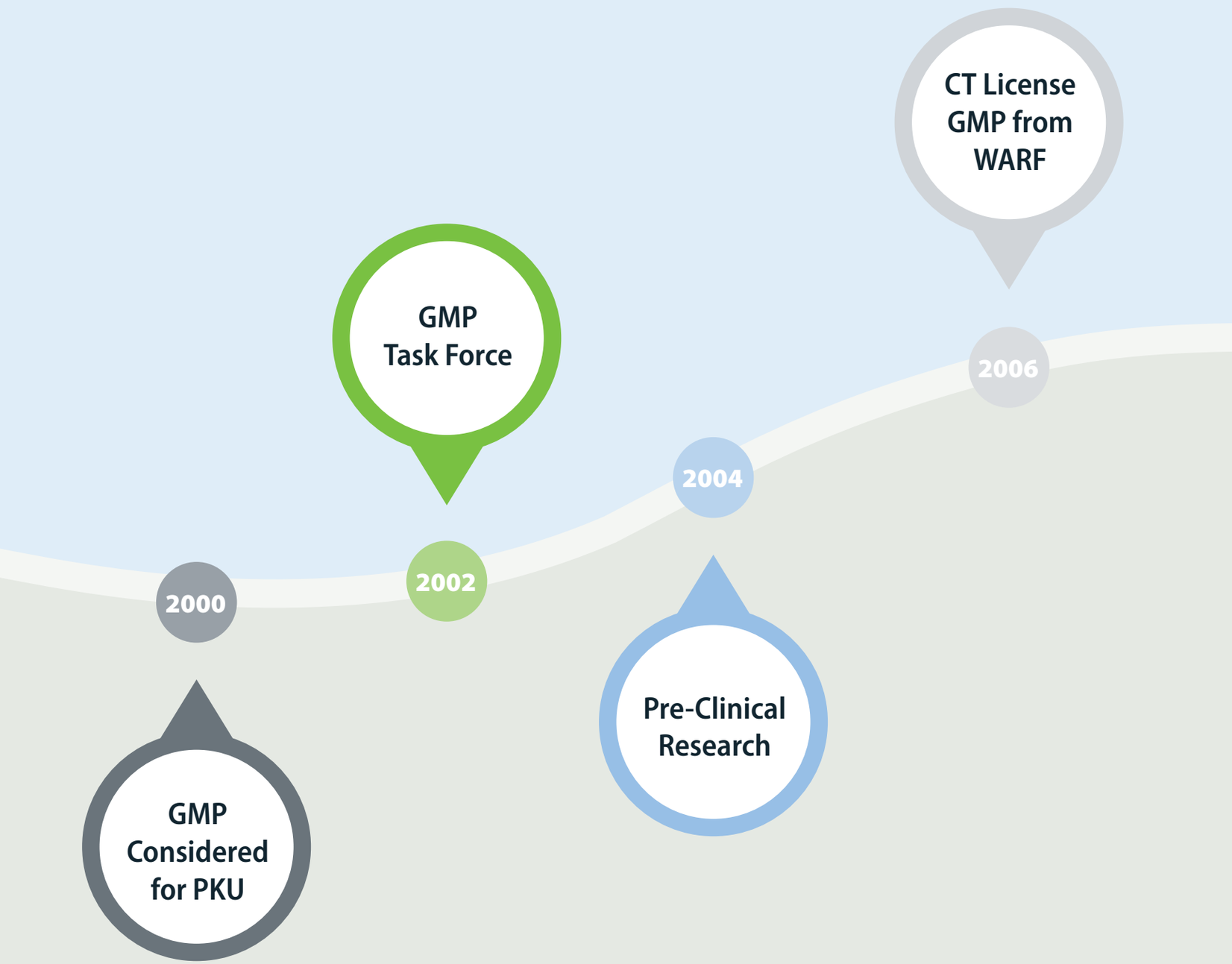
Build 20/20 RTD Lite

2018

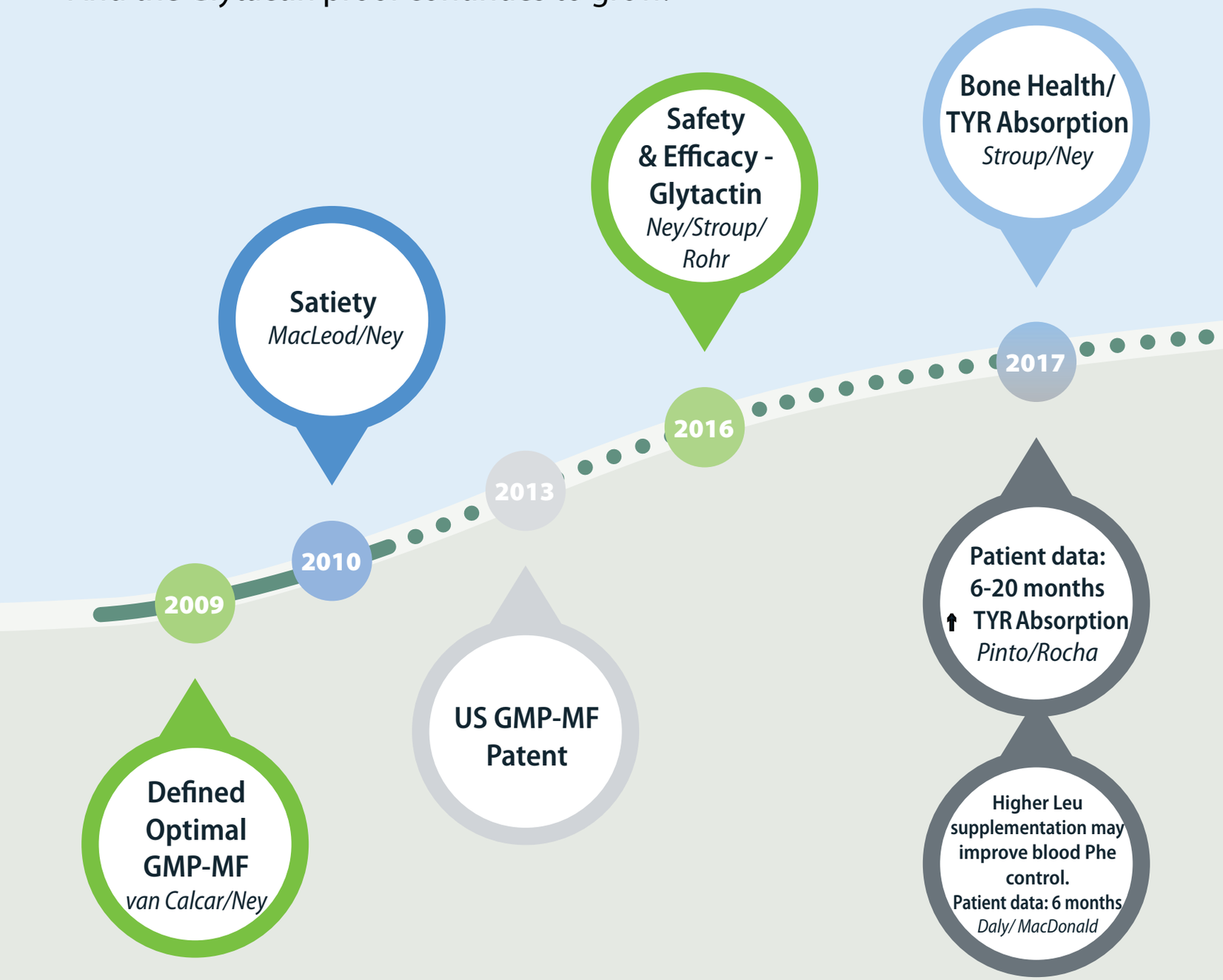
The only **GMP formula with 1mg Phe/g PE**

Discovering GMP Was Good, but Not Good Enough

Over 10 years of pre-clinical and clinical studies led to the purposeful design of Glytactin (GMP).



And the Glytactin proof continues to grow.



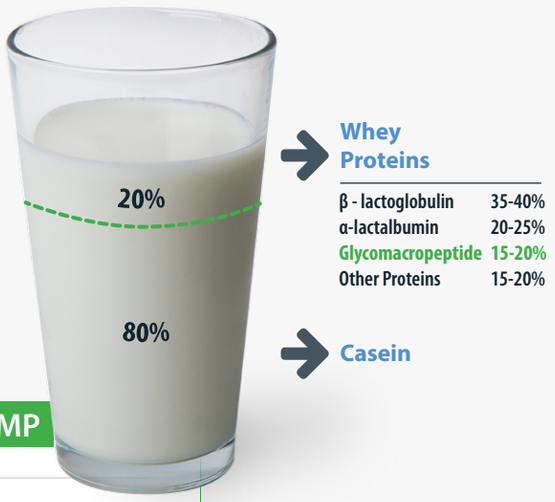
First Experimental GMP-MF

Glytactin - MF

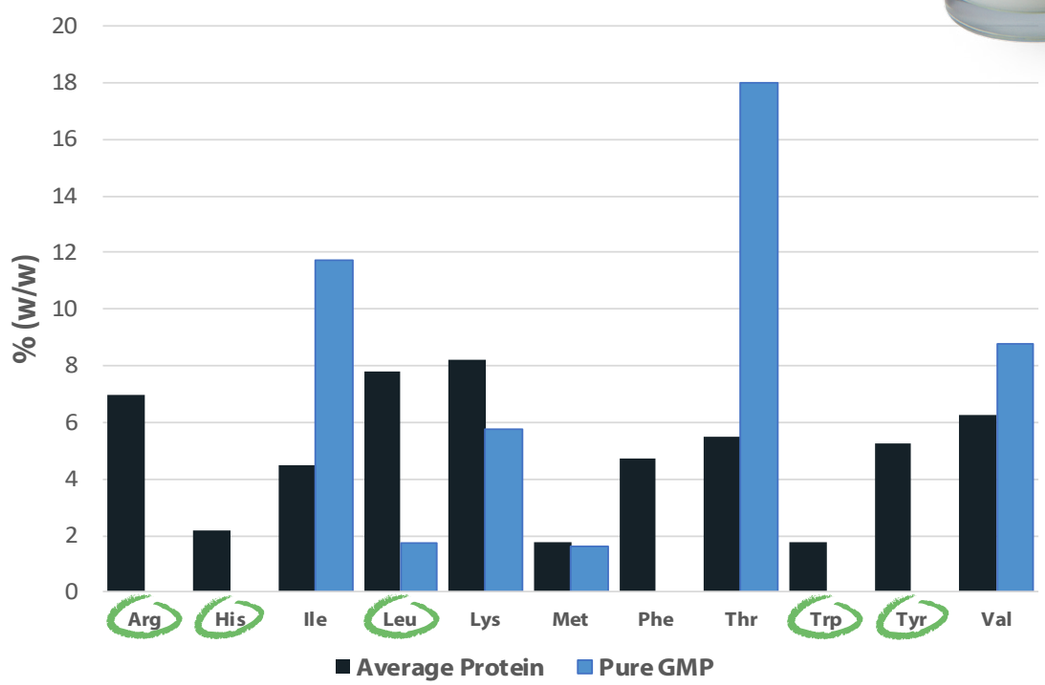
Empirical Proof of Concept: Balancing AAs

What We Now Know: GMP Must Be Supplemented

- GMP is an intact whey protein found in milk
- Pure GMP contains no Phe
- GMP must be supplemented with 5 limiting amino acids

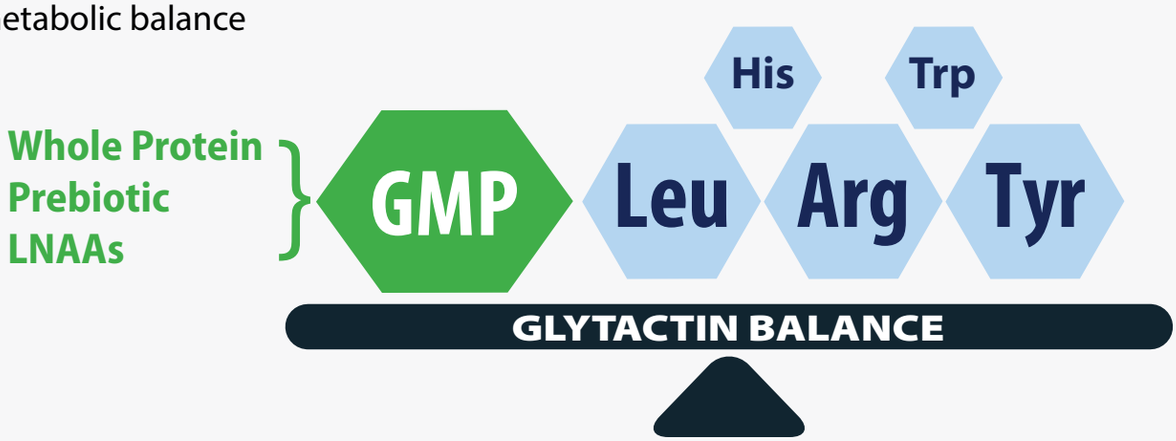


Essential/Conditionally Essential AA Profile: Whole Protein vs GMP



Staying a Step Ahead: Rigorous Science Led to Today's Glytactin Design

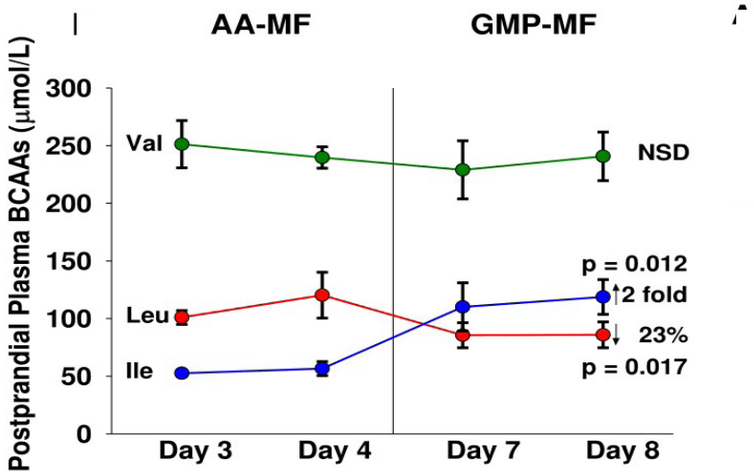
GMP must be balanced with 5 AAs
to achieve metabolic balance



To Achieve Plasma BCAA Balance, Evidence Suggests Leu Supplementation Needs to Be 2 x Ile

First experimental GMP formula was supplemented with Leu:Ile at 1:1, resulting in suboptimal plasma levels:

Postprandial Plasma BCAAs with Consumption of Experimental GMP-MF



AA-MF mg/g PE		GMP-MF mg/g PE	
Val	76	Val	84
Leu	117	Leu	72
Ile	66	Ile	104
Leu:Ile	1.7	Leu:Ile	0.7

Subsequent postprandial concentrations of BCAAs in plasma 2.5 hours after breakfast. — van Calcar, et al. Am J Clin Nutr, 2009

- WHO Protein Recommendation: Leu 2 x requirement for Ile, 2:1
- **Glytactin formulas supplemented with proven LEU:ILE (2+:1) resulting in optimal plasma BCAA levels — Ney 2016**

Potential risks to insufficient Leu supplementation:

Limits Protein Synthesis → Protein Degradation ↑ + Phe ↑ → **Impaired Growth**

Staying a step ahead…

Glytactin Product Evolution: Our Portfolio Grew as the Science Advanced

Staying a step ahead

Since developing GMP medical foods in 2010 and being the first to see its potential, we have focused our resources on making it even more balanced.

And it is just the beginning

20 20

BUILD 20/20 *flavors*

Because it is our mission

To us, it is all about helping people living with PKU balance their lives with advanced formulas and delicious low protein foods.

LET NOTHING STAND IN YOUR WAY

NEW

GLYTACTIN®

20 BUILD

Flavors

- 110 calories per 20g PE
- 20mg Phe per 20g PE
- Mix with 120ml water
- 4 delicious flavours

Feel balanced. Feel better.™

Glytactin BUILD 20/20 now available in four delicious flavours!

Order your variety kit today!

RASPBERRY LEMONADE

SMOOTH

VANILLA

CHOCOLATE

Additional Features

- Complete with vitamins and minerals
- Contains DHA, Calcium, Vitamin D and probiotics
- No artificial colours or flavours

GMP Powdered Formulas for PKU

Per 20 g PE	BUILD 20/20 *flavors*	BUILD 20/20	PKU sphere20 Red Berry
Calories	110	100	120
Carbs, g	2	1	6.3
Calcium, mg	540	532	353
Vitamin D, mcg	14	14.5	4.2
Vitamin K2, mcg	18	18	0
Mixing Volume, ml	120	180	120
Phe, mg	20	20	36

* Compared to flavoured formulas

Eat Well. Live Well.
AJINOMOTO

CAMBROOKE™

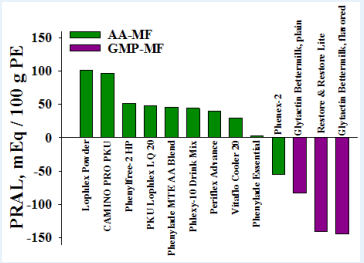
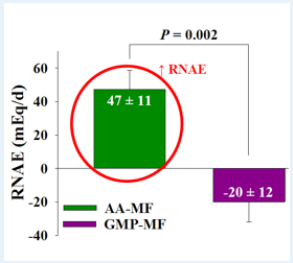
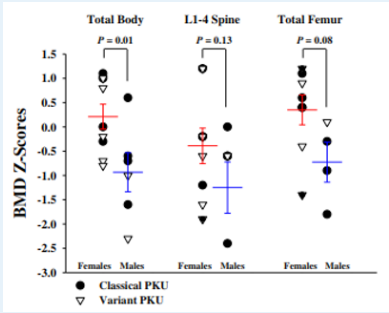
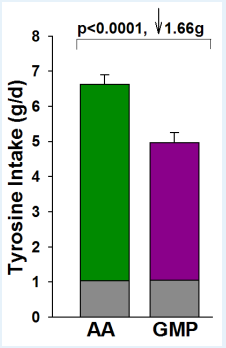
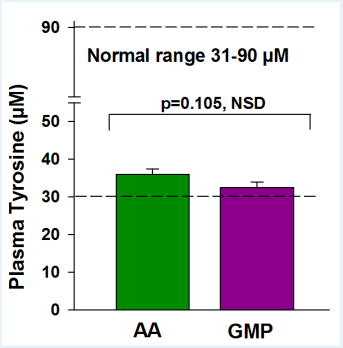
866 456 9776 cambrooke.com info@cambrooke.com

© Ajinomoto Cambrooke, Inc. All Rights Reserved. R112520

GLYTACTIN RESEARCH SUMMARY

CAMBROOKE THERAPEUTICS™

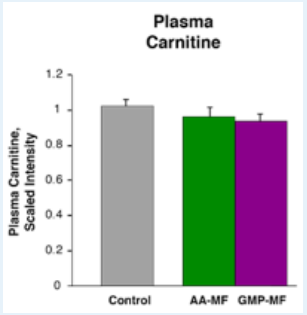
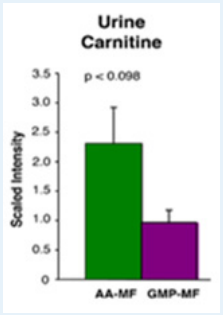
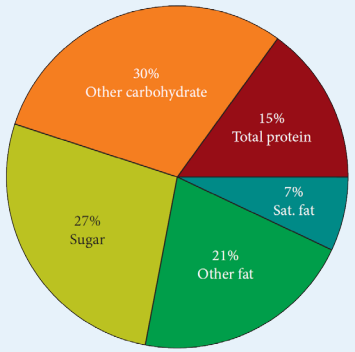
Additional Data Insights from the 30 subject Prospective, Randomized, Crossover Study (Ney DM, et al. – AJCN 2016).

Study	Participants & Analysis	Findings	Supporting Data	Conclusions by Authors
Stroup BM, et al. Amino acid medical foods provide a high dietary acid load and increased urinary excretion of renal net acid, calcium, and magnesium compared with glycomacropeptide medical foods in phenylketonuria. J Nutr Metab. 2017 May; 2017:1909101 PMID: 28546877	Subset of 8 participants • Ages: 16-35 years • Gender: 4 females, 4 males • Classical PKU (n=4) Variant PKU (n=4) • Excess body fat: 2 females, 3 males **Data collected:** • 3-day food diaries for each arm of study • Dietary acid loads of all medical foods utilized in the study • 24-hour urine samples	• 25% of participants had low Bone Mineral Density-for-age, both were males • Dietary protein, calcium, and magnesium intake were similar • AA-MF provided 1.5–2.5-fold higher Potential Renal Acid Load (PRAL) and resulted in 3- fold greater renal net acid excretion • **Urinary excretion of calcium and magnesium were reduced by 40% and 30% respectively while consuming Glytactin GMP-MF**	 	• The high dietary acid load of AA-MF likely contributing to the etiology of skeletal fragility in PKU • Glytactin GMP-MF promotes retention of calcium and magnesium which can then be used for bone mineralization
Stroup BM, et al. Sex differences in body composition and bone mineral density in phenylketonuria: a cross-sectional study. Mol Genet Metab Rep 15 (2018) 30-35	Subset of 15 participants • Ages: 15-49 years • Gender: 9 females, 6 males • Classical PKU (n=8) Variant PKU (n=7) • Participants reported life-long compliance with AA-MF **Data collected:** • DXA scan evaluated to determine impact of AA-MF on bone mineral density	• Only 50% percent of male participants had total body BMD Z-scores above −1.0 • Males tended to consume more grams of protein equivalents per day from AA-MF than females (means ± SE, males: 67 ± 6 g, females: 52 ± 4 g) • Males showed a trend for higher urinary calcium excretion compared to females • Males had a low-normal lean mass based on the appendicular lean mass index (ALIM), but were similar to the female participants		• Males with PKU have lower BMD compared with females with PKU which may be related to higher intake of AA-MF and greater calcium excretion • Calcium and magnesium excretion is lower with Glytactin GMP-MF
Ney DM, et al. Metabolomic changes demonstrate reduced bioavailability of tyrosine and altered metabolism of tryptophan via the kynurenine pathway with ingestions of medical foods in phenylketonuria. Mol Genet Metab. 2017 Jun;121(2):96-103. PMID 28400091	Subset of 18 subjects • Age: 15-49 years • Gender: 10 females, 8 males • Classical PKU (n=11) • Variant PKU (n=7) **Data collected:** • Metabolomic analysis was conducted on plasma (n= 18) and urine (n= 9) samples	• **Intake of Tyr and Trp was ~50% higher with AA-MF but concentrations in the blood were not significantly different** • For subjects with variant PKU, plasma serotonin levels were 3-fold higher and these levels increased with ingestion of Glytactin GMP-MF • Urinary excretion of tyramine (headaches) and phenol sulfate (nephrotoxic) were 50–90% higher with ingestion of AA-MF • With AA-MF, a greater portion of Tyr is metabolized through the kynurenine pathway which is associated with inflammation-related neuropsychiatric diseases	 	• Bioavailability of Tyrosine and Tryptophan are improved with Glytactin GMP-MF, possibly due to the prebiotic properties of GMP • Glytactin GMP prevents the diversion of Trp away from serotonin synthesis thus increasing plasma levels and reducing the inflammatory response

© Cambrooke Therapeutics, Inc. All Rights Reserved R040918

GLYTACTIN RESEARCH SUMMARY

CAMBROOKE THERAPEUTICS™

Study	Participants & Analysis	Findings	Supporting Data	Conclusions by Authors
Stroup BM, et al. Metabolomic markers of essential fatty acids, carnitine, and cholesterol metabolism in adults and adolescents with phenylketonuria. J Nutr 2018;148:194-201 PMID: 29490096	• **Study design 1:** Analyzed the Fatty Acid (FA) profiles of Red Blood Cell Membranes in 25 adult subjects with classical and variant PKU and 143 controls • **Study design 2:** Metabolomics analysis of plasma samples of 10 adults and adolescents with PKU compared to age-matched controls • **Study design 3**: Metabolomics analysis of urine samples of 9 adults and adolescents with PKU	• PKU subjects had higher n-6/n-3 ratio in RBC and plasma oxidized derivatives of 18:2n-6 and lower ratio of 20:4n-6/20:3n-6 in RBC, consistent with compensation for inflammation • **Despite higher L-carnitine intake from AA-MF, plasma carnitine is similar between AA-MF and Glytactin GMP-MF** • Urine excretion of carnitine and trimethylamine N-oxide (TMAO) was higher with AA-MF	 	• Bioavailability of L-carnitine is improved with Glytactin GMP-MF, possibly due to the prebiotic properties of GMP • Lower TMAO levels with Glytactin GMP-MF may indicate reduced risk for atherosclerosis and cardiovascular disease
Stroup BM, et al. Metabolomic insights into the nutritional status of adults and adolescents with phenylketonuria consuming a low- phenylalanine diet in combination with amino acid and glycomacropeptide medical foods. J Nutr Metab. 2017 Dec; 2017:6859820. PMID 29464117	30 adult and adolescent subjects with classical and variant PKU • Ages: 15-49 years • Gender: 18 females, 12 males • Classical PKU (n=20) • Variant PKU (n=10) **Data collected:** • Analysis of micronutrient intake utilizing 3 day food records from each arm of intervention • Fasting Phe levels • Metabolomic analysis of plasma and urine	• Intake for sugar was excessive at 27% of total energy (goal <10%) for both AA-MF and Glytactin arms • Macronutrient composition of the low-Phe diet did not change between AA-MF and Glytactin arm of the study • Inadequate intake of Potassium and Choline with both AA-MF and Glytactin GMP-MF • **If taking MF without micronutrient supplementation >70% of participants would have inadequate intake of 11 micronutrients: biotin, choline, pantothenate, Vitamin D and E, potassium, calcium, iodine, magnesium, selenium, and zinc** • Content of sulfur containing AA's in AA-MF are 3x higher than WHO recommendations	Macronutrient Composition of Low-Protein Diet plus Medical Foods  Inadequate and Excessive Intakes as a Percentage of Subjects | | <AMDR or DGA | >AMDR or DGA | |---|---|---| | Total protein | 7% | 0% | | Total carbohydrate | 10% | 20% | | Sugar | — | 97% | | Total fat | 17% | 17% | | Saturated fat | — | 13% |	• Medical foods containing less sugar (like the new Glytactin RTD Lite, Build, Restore Lite, and BetterMilk Lite products) are needed for the PKU community • Vitamin and mineral supplementation of medical foods, like in Glytactin's complete GMP–MF, is necessary in order to prevent nutrient deficiency in PKU • Per the original study, compliance with completion of MF was 1.5 fold higher with Glytactin MF thus promoting improved micronutrient intake

© Cambrooke Therapeutics, Inc. All Rights Reserved R040918