Global Report on Obesity

Survey of Market Participants and Emerging Technologies in Obesity

Module #1
What's What. Clinical need, Obesity challenges and current standards of Care.
In this report we provide an understanding of Obesity's epidemiology, the current treatments, trends worldwide, relative benefits of treatments, and the direction of future treatments.

Module #2
What's Now. Current Players and Market Structure.
Here we take a look at the current marketplace; the current players, market share, treatments options, mechanisms of action. Complete review of drugs on the market today, their relative strengths and weakness, with profiles of the leading competitors and their technologies.

Module #3
What's Next. Future Players and Technologies.
This report anticipates a future marketplace by way of new and emerging technology-based companies. We assess their conceptual strengths, weaknesses, and approval expectations to evaluate prospects for success.

Module #4
Who's Who. The Ecosystem. Directory of Important Institutions and Individuals.
The directory comprises an invaluable resource to understand the important competitors and the roles they play in the overall ecosystem. Includes: organization, key contact information, analysis, major events, publications, key management biographies for all the important investment houses, associations, publications, research institutions, foundations and thought leaders.

OneMedResearch

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OneMedResearch

Global Report on Obesity

Obesity's intensification and increasing cost to the health care system composes a growing epidemic. An estimated 30% of the US population is considered obese with 6% marked severely or morbidly obese. The combined comorbidities of obese patients are collectively regarded as the biggest single drain on the country's health care system, which is an estimated $300 billion annual bill.

Yet despite the problem's size, there has been little in the way of new drugs coming to market. The total count is two approved drugs in the last five years and none in the preceding 13 years.

The objective of this research report is to identify the new opportunities and give investors an overall understanding of the obesity market. The full report which is packaged into four sections, contains insight on:

- 32 companies with obesity drugs in development.
- 11 drugs at some stage of the FDA approval. (US only).
- 21 distinct drug targets with non-scientific summaries.
- 18 mechanism of action (MOA) with summaries.

The report also includes profiles of seven promising new entrants as a look at the major actors serving this market:

- 14 venture, private equity funds with active investments.
- Business development contacts and major strategic investors.
- 24 professional groups, non-profits, associations, media outlets and influencers.

We have a master report which totals 50 pages 140 citations which is then divided into 4 separate reports:

1. **What's What.** The need, challenges current status.
2. **What's Now.** Current players and market structure.
3. **What's Next.** Future players and technologies.
4. **Who's Who.** Directory of important institutions and individuals.

ABOUT**:** OneMedResearch is the research group of OneMedMarket LLC which manages the OneMedForum investment conferences, OneMedMedia and OneMedPlace (www.onemedmarket.com).

The research was conducted between April and July of 2015 by a team of PhD Candidates at leading Universities in addition to by staff at OneMedReseach in New York. The team included: Katie Smolnycki, Prashant Monian, Oluseyi O. Fasoranti, Margaret Elvekrog. Senthilkumar Sivagurunathan was the Project Manager and Jasmin Siegle, Project Advisor. Staff Researcher include Taylor Kinze and Julia Berdecia and Brett Johnson as Managing Director.

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We encourage readers to make suggestions and if possible alert us to additional companies or technologies that may be imminent. An update to this report planned for Release in late October 2015.

For additional information about the report and research services contact us at tkinze@onemedmarket.com or visit www.onemedmarket.com.

Module 3: What's Next

What's Next. Future Players and Technologies. This report will look at the future expected marketplace. The new and emerging companies and the technologies being developed, drug targets and mechanisms of action. Strengths and weaknesses of their concepts and expectations as to approvals as well as profiles of the leading players, their technologies and prospects for success.

Drugs in the Approval Pipeline

New entrants that are currently developing anti-obesity drugs can be broadly classified into two groups.

1. **Phase III.** This group consists of drugs currently undergoing clinical trials, and that also look promising with a strong possibility of entering the market soon (Phase III Drugs).

2. **Preclinical, Phase I and Phase II.** The final group consists of drugs that are currently undergoing clinical investigation or are in development, but have not at this point provided well-developed data on efficacy and safety in humans for obesity treatment (Preclinical, Phase I and Phase II Drugs). We will discuss these three groups in the next section:

Phase III Drugs & Promising Phase II Drugs

frontrunner. Beloranib was licensed from OKI Pharma. Zafgen raised over $115 million from investors before going public in June 2014.

Beloranib (ZGN-440) is a novel obesity therapy that is a methionine aminopeptidase (MetAP2) 1 inhibitor- an enzyme that helps produce fatty acids. MetAP2 inhibitors work by reestablishing balance in the way the body stores and utilizes fat. Inhibitors of MetAP2 reduce the generation of new fatty acid molecules in the liver and help convert stored fats into energy. Beloranib targets this enzyme and restores balance to the production and metabolization of fat leading to positive metabolic changes. Beloranib is interesting in that, while current drugs are expected to trick the body into thinking that it is full, this drug will change the way the body metabolizes fat. The most common side effects seen in clinical studies are nausea, vomiting and diarrhea, with no serious side effects arising. They have received funding to the tune of $155.2 million in 7 Rounds from 9 Investors. Their investors include Atlas Venture, Greatpoint Venture, Third Rock Ventures, Alta Partners, RA Capital Management, Brookside Capital, Vennock, MidCap Financial, and Oxford Finance Corporation.[1]

Zafgen has initiated Phase III trial for their beloranib drug in October 2014. The "best PWS" trial (Beloranib Efficacy Safety and Tolerability in PWS), is a randomized, double-blind, placebo-controlled trial in obese adolescents (12 years of age and older) and adults with Prader-Willi syndrome to evaluate food-related behaviors, total body fat mass, and safety of beloranib. The "bestPWS" trial is expected to enroll 84 patients at 14 different sites across the United States.[1] One issue with Zafgen's clinical studies is the sample size, with participants in the study roughly numbered at 120 compared to other anti-obesity clinical studies where the sample size > 1000. This raises questions about the efficacy of their drug when exposed to a larger sample size as well as if the safety profile will change if the drug is administered to a population size with a broader metabolic profile.

Rhythm Pharmaceutical is another company that has shown promise in the development of a novel anti-obesity drug. Rhythm is a biopharmaceutical company that is involved in the development of peptide therapeutics. They have received a total of $94.9 million from 6 investors. In the most recent fund round in September 2013 they obtained $1.4 million. They have received significant investment support from the Michael J. Fox Foundation (Parkinson Research), Third Rock Ventures, Ipsen, New Enterprise Associates, MPM Capital, Pfizer Venture Investments.[1]

Their drug candidate RM-493 is a melanocortin (MC4) receptor agonist. It has been proposed that genetic defects in the MC4 gene could cause obesity.[1] Previous studies using other MC4 agonists were not productive, since they caused increases in blood pressure. RM-493 on the other hand is quite safe and retains the specificity and functionality of the naturally occurring hormone, which activates MC4. Additionally, RM-493 does not appear to effect blood pressure based on Phase I clinical trials. They commenced Phase II clinical trials in January 2013,[1] with this trial being designed to evaluate the effect of RM-493 on weight loss and safety in obese subjects treated for three months. The trial also assessed the effect of the drug on glucose and insulin resistance. With this trial being completed last month, initial results show that the RM-493 increased energy expenditure significantly.[1] It has been suggested that RM-493 could achieve double-digit weight loss. Primates treated for 8 weeks lost an average of 13.5%. The RM-493 is administered via subcutaneous injection.

Ember Therapeutics is another company that has a promising portfolio of drugs for obesity treatment. They recently merged with Mariel Therapeutics so as to enlarge their drug portfolio. The company was formerly known as Adipothermics Inc. and then changed its name in 2011. They were founded by Third Rock Ventures with $34 million investment, but had to shutdown in December 2014. However, in 2015, Ember merged with Mariel Therapeutics, a company focused on developing osteoarthritic therapies and became a combined entity under the name Ember Therapeutics.[1] Their drugs work through the brown fat mechanism and include PRDM16, Foxc2, TRPV4, Therm1 and Aldh1a1. Studies have shown that inhibition of Aldh1a1 induced classic brown fat characteristics, including increased expenditure, lowered glucose levels and weight gain. Also other studies have demonstrated that Therm1, a long chain fatty acyl-CoA thioesterase that is highly enriched in brown fat, plays an important role in regulating energy homeostasis.[1] BMP7 is active in stimulating brown fat development.

TABLE 10: FDA Approved & Phase I/II/III companies that are poised enter in the obesity drug market.[77,78]

Mechanism of Action		Company	Drug	Target	Status
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Abbreviation list:

[illegible]

[illegible]

Mechanism of Action

❶ **MC4 pathway**, an important cell signaling mechanism is involved in the regulation of energy expenditure, homeostasis, and appetite. Genetic defects in the genes associated with in MC4 pathway leads to early-onset and severe obesity confirming MC4's role in weight regulation.[79]

❷ **Neuropeptide Y (NPY)** is a potent appetite stimulating (orexigenic) neuropeptide, and blockade of its cognate receptors NPY Y1 and NPY Y5 (NPYxR) is considered an important anti-obesity drug target.[80]

❸ **Byetta** suppresses appetite by delaying the movement of food from the stomach into the small intestine leading to a feeling of satiety and reduced appetite.

❹ **Obinepitide** is an analog of two peptide hormones that are associated with food intake and appetite regulation and are known to play a role as satiety signals.[81]

❺ **Lipase Inhibitors** such as Cametor (Cetilistat) inhibits the activity of lipase, a lipolytic enzyme, secreted by the digestive tract and pancreas, and block the absorption of fat from the gut, resulting in reduced body weight.[82]

TABLE 11: Company Profile of New Entrants in the Market

Companies	CEO	Year Founded	Location	Drug	Funds Raised	Investors	Drug Phase	Mode of Administration
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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Companies	CEO	Year Founded	Location	Drug	Funds Raised	Investors	Drug Phase	Mode of Administration
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Pre-Clinical Innovations on Horizon

There are several companies that are currently working on developing anti-obesity drugs. The efficacy and safety of these drugs have not been significantly proven clinically, but they have the potential.

These companies are summarized in **Table 11**. The most promising of these companies are 7TM Pharma, Zealand Pharma A/S, Obetal Pharma and Intarcia Therapeutics.

7TM Pharma is located in Copenhagen, Denmark. It is focused on developing new drugs that target 7TM receptors. Their lead compound is Obinepitide, which targets the treatment of obesity, is in Phase II clinical study. Obinepitide (TM30338) is a synthetic analogue of two natural human hormones, PYY3-36 and pancreatic polypeptide PP, which are normally released during food consumption. They also recently announced that a second obesity compound entered Phase I/II studies in early 2008. This drug, TM38837 is a first in class, second generation CB1 receptor antagonist. Another drug in their portfolio is TM30339, which is a selective Y4 receptor antagonist, and is currently in clinical development Phase I/II for treatment of obesity.[xx]

Zealand Pharma A/S is also another small company that is focused on type 2 diabetes and obesity and is poised to provide some novel obesity solutions. Their main drug target for obesity is ZP1529, which is currently undergoing Phase I study. ZP1529 is a once daily dual acting glucagon/GLP-1 peptide receptor agonist for subcutaneous administration. Zealand A/S Pharma has partnered for the commercialization of its obesity pipeline with Boehringer Ingelheim and Eli Lilly.[xx] ZP1529 will be similar to Saxenda, in mechanism, though it would be interesting to see if there are any significant changes in the drug efficacy profile.

Obetal Pharma has developed a peptide with rapid and substantial weight loss efficacy with a novel Mechanism of Action. It increases PGC-1 in muscle and UCP1 in white adipose tissue which turns white fat into brown fat. The origins for the drug started about a decade ago. Prof. Man-Wook Hur, PhD (Medical School of Yonsei University, Seoul, Korea) initiated extensive researches and experiments with Tat protein, a small protein encoded by HIV that is essential for viral replication ("Tat" stands for Trans activator of transcription). Dr. Hur's research have shown that the small Tat protein alone can induce a dramatic weight loss in animal models, mimicking the wasting syndrome observed in untreated AIDS victims. They have seen as much as 25% weight reduction, all most all of them from reduction of fat, in animal studies.

Intarcia Therapeutics is another small company that currently has some anti-obesity drugs in its pipeline. Intarcia is different from the other companies listed in that it is also a drug delivery company. They have developed a subcutaneous mini-pump technology to address some of the primary obstacles that are encountered in developing safe drug therapies in obesity. This drug delivery method employs the "DUROS drug delivery platform" and will be paired with some of their peptide technologies. They are headquartered in Hayward, CA. Intarcia is evaluating a series of human peptides for delivery with its mini-pump technology.[xx]

Another interesting company that needs to be noted is **Rezlet Therapeutics**. Rezlet Therapeutics has developed a novel drug that after a single injection into subcutaneous fat will convert white adipose tissue (WAT) into brown adipose tissue (BAT). The name of Rezlet's drug candidate is RZL-12 which is a potential first in class, injectable drug currently in pre-clinical development for the reduction of fat cell mass.[xx] They are also assessing the feasibility of making this drug available in an oral form. Their main investor is VLX (Van Leer Xenzo) Ventures. This is quite similar to the drug being made by Obetal.

Furthermore, small subsets of companies are developing anti-obesity drugs, but are relative unestablished at this point. They are using novel methodologies to address obesity. One of these is **Compellis Therapeutics** whose candidate drug CP404 is a calcium channel blocker used in a nasal formulation to block olfactory activity and reduce food intake.[92] As a result it can be classified as an anorexic drug. The advantage of CP404 is that it is a small molecule that is well tolerated in humans and is readily manufactured. Based on its prior use in humans for certain other disorders, Compellis believes it will be eliminating some of the drawbacks typically associated with unproven compounds. They have started human testing in 2007. There are companies like **Inscannex Therapeutics ApS**, whose main therapy is the Vpx32p-receptor derived peptides and proteins that could potentially be used for treating obesity.

Another worthy mention is **Versa Pharmaceuticals**, which is also developing a new set of drugs that are referred to as "versa fat blockers." At the moment they have generated preclinical proof of concept with two obesity technologies that will prevent de novo fat cell formation. They recently discovered that compounds that will act as versa targets were found to reduce body fat and body weight in obese mice and prevented fat as well as weight gain in lean mice placed on a high fat diet. Although no human trials have been performed, it is expected that these fat blockers will reduce fat cell number leading to a better endocrine profile and reduced appetite.

Also since these fat blockers do not act on the CNS, they will avoid some of the side-effects associated with current drugs on the market. It is expected that this technology will also have several therapeutic indications including the prevention of weight gain in general, regaining of fat after weight loss and drug-induced weight gain.[93]

The drugs in **Table 12** are either in the research phase in which lead identification is currently being done or in the preclinical stage. These drugs have been indicated for both type 2 diabetes and obesity in animal models, but not in a human trial model.

TABLE 12: Companies that have Obesity Drugs in the Pipeline

Company	Drug Target	Phase	Location	MOA	Notes
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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Company	Drug Target	Phase	Location	MOA	Notes
[illegible]	[illegible]	Preclinical	[illegible]	[illegible]	
[illegible]	Not disclosed	Preclinical	South Korea	Not disclosed	Collaboration with Takeda Pharmaceuticals
[illegible]	[illegible]	Phase II	Japan	Sodium-glucose transporter 2 (SGLT2) inhibitor	Has shown clinical efficacy in weight loss in 2013. Has been approved for Type 2 Diabetes
[illegible]	Tesevilgliptin	Preclinical	Osaka, Japan	DPP-4 Inhibitor (dipeptidyl peptidase-4 inhibitor)	
[illegible]	Not disclosed	Preclinical	Memphis, TN	β3- selective agonist	
[illegible]	LIPO-222	Phase IIa (2015)	San Diego, CA	β3-adrenergic receptor agonist	Injectable drug for reducing belly fat. Aesthetic company and not focused on severe obesity.
[illegible]	Nucleic Acids (nano-oligomers)	Preclinical	Barcelona, Spain	Targeting neuronal PTP1b in Hypothalamic AGRP neurons	Still in the research phase with patent expected in 2016
[illegible]	Peptides	Preclinical	Copenhagen, Denmark	NA	Early research going on in US.
[illegible]	Hindawan (formerly OMC-101)	Phase II (A)	Ramat Gan, Israel	Anti-obesity compound comprised of betahistine	Obecure Phase II Trial showed positive results in 2007
[illegible]	TZP-301	Preclinical	Durham, NC	Ghrelin antagonist	Tranzyme Pharma owns right to TZP-301 but was purchased by Ocera Therapeutics
[illegible]	MCR3/4R agonist	Preclinical	Cranbury, NJ	Melanocortin receptor (MCR) agonist that creates anorexic effect	
[illegible]	PYM22 (monoflavin)	Preclinical	Oxfordshire, United Kingdom	Purified Plant Extract	
[illegible]	PM022003	Phase II	Cambridge, UK	Serotonin (5-HT2C) receptor agonist	

Company	Drug Target	Phase	Location	MOA	Notes
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Mechanism of Action

❶ **Melanin concentrating hormone (MCH)** is an appetite stimulating peptide that affects food intake and body weight regulation. MCH peptide regulates energy homeostasis through the MCH1 receptor by stimulating feeding and promoting glucose, insulin and leptin levels. Blocking MCH1 receptor reduces food intake in rats and leads to body weight and fat stores reduction.[92]

❷ **Leptin,** is a hormone made exclusively by fat cells, regulates both metabolism and appetite. Leptin resistance is a proposed reason for obesity. One cause of leptin resistance is the impaired transport of leptin receptors through the blood-brain barrier. A leptin therapy that can effectively transport across the blood-brain barrier could prove effective in treating obesity.

❸ **Somatostatin** vaccine induces body's immune system to produce anti-somatostatin antibodies and thus inhibiting its function. Somatotatin functions by antagonzing growth hormone and insulin-like growth factor, both of which increase metabolism, fat breakdown, and muscle build-up leading to weight loss.[93]

❹ **ZAG** is an adipokine (cell signaling proteins) secreted by adipose (fat) tissue involved in the mobilization and utilization of fat and thus plays a key role in fat cell metabolism.[94]

❺ **Ghrelin** is involved in appetite stimulation, suppression of insulin secretion and weight gain via its receptor GH secretagogue receptor type 1a (GHS-R1a). Antagonists to ghrelin receptors may reverse its effects.[101]

❻ **MC4 receptor** is associated with feeding behavior and energy homeostasis. It has been shown that agonists (eg., alpha-MSH) exert anorectic effects similar to the mechanism of Rhythm's RM-493.

Some of the drugs we listed in **Table 12** have a lot of potential if they are able to show efficacy in future clinical studies. Also observed is the emergence of nucleic acid technology such as nLife Therapeutics and ISIS "ISIS-FGFR4RX" to target obesity.

Product Comparison/Differentiation

The new entrants to the market are comprised of both peptide and small molecule drugs.* These new generation compounds act by inducing anorectic and/or fat burning effects via a wide variety of cellular mechanisms as shown in **Table 13**.

TABLE 13: Comparison of New Entrants in the Market

Company (Compound)	Molecule Type	Mode of Administration	Effect	Mechanism of Action	Price	Clinical Stage
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Company (Compound)	Molecule Type	Mode of Administration	Effect	Mechanism of Action	Price	Clinical Stage
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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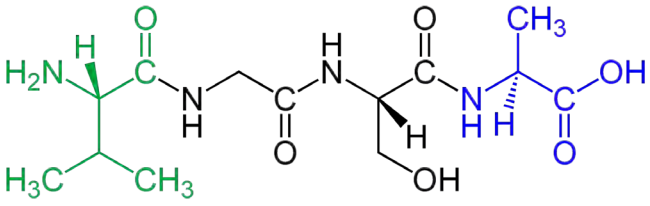
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Abbreviation list:

[illegible]

Note on Peptides & Small Molecules

*Peptide drugs offer high efficacy, high specificity, lower toxicity, and a wide range of target selectivity in contrast to small molecule drugs. However, small molecules exhibit higher stability, oral bioavailability, and lower production costs. Due to these characteristics peptide drugs are usually administered parenteral (subcutaneous injection) in contrast to orally administered small molecules.[102]



Peptides (from Gr. **πεπτός**, "digested", derived from **πέσσειν**, "to digest") are naturally occurring biological molecules. They are short chains of amino acid monomers linked by peptide (amide) bonds. The covalent chemical bonds are formed when the carboxyl group of one amino acid reacts with the amino group of another. The shortest peptides are dipeptides, consisting of 2 amino acids joined by a single peptide bond, followed by tripeptides, tetrapeptides, etc. A **polypeptide** is a long, continuous, and unbranched peptide chain. Hence, peptides fall under the broad chemical classes of biological oligomers and polymers, alongside nucleic acids, oligosaccharides and polysaccharides, etc.

Peptides are distinguished from proteins on the basis of size, and as an arbitrary benchmark can be understood to contain approximately 50 or fewer amino acids. Proteins consist of one or more polypeptides arranged in a biologically functional way, often bound to ligands such as coenzymes and cofactors, or to another protein or other macromolecule (DNA, RNA, etc.), or to complex macromolecular assemblies. Finally, while aspects of the lab techniques applied to peptides *versus* polypeptides and proteins differ (e.g., the specifics of electrophoresis, chromatography, etc.), the size boundaries that distinguish peptides from polypeptides and proteins are not absolute: long peptides such as amyloid beta have been referred to as proteins, and smaller proteins like insulin have been considered peptides.

Note on Small Molecules

In molecular biology and pharmacology, a **small molecule** is a low molecular weight (<900 daltons) organic compound that may help regulate a biological process, with a size on the order of 10^{-9} m. Most drugs are small molecules.

The upper molecular weight limit for a small molecule is approximately 900 daltons, which allows for the possibility to rapidly diffuse across cell membranes so that they can reach intracellular sites of action. In addition, this molecular weight cutoff is a necessary but insufficient condition for oral bioavailability. Finally, a lower molecular weight cutoff of 500 daltons (as part of the "rule of five") has been recommended for small molecule drug development candidates based on the observation that clinical attrition rates are significantly reduced if the molecular weight is kept below this 500 dalton limit.

Pharmacology usually restricts the term to a molecule that binds to a specific biopolymer—such as protein or nucleic acid—and acts as an effector, altering the activity or function of the biopolymer. Small molecules can have a variety of biological functions, serving as cell signaling molecules, as drugs in medicine, as pesticides in farming, and in many other roles. These compounds can be natural (such as secondary metabolites) or artificial (such as antiviral drugs); they may have a beneficial effect against a disease (such as drugs) or may be detrimental (such as teratogens and carcinogens). Biopolymers such as nucleic acids and proteins, and polysaccharides (such as starch or cellulose) are not small molecules—though their constituent monomers—ribo- or deoxyribonucleotides, amino acids, and monosaccharides, respectively—are often considered small molecules. Very small oligomers are also usually considered small molecules, such as dinucleotides, peptides such as the antioxidant glutathione, and disaccharides such as sucrose.

Small molecules may also be used as research tools to probe biological function as well as leads in the development of new therapeutic agents. Some can inhibit a specific function of a multifunctional protein or disrupt protein-protein interactions.

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