Autism and Autism Spectrum Disorders are characterized as mental disorders associated with self-absorption, inability to interact socially, as well as behavioural and lingual dysfunctions. Despite these distinct impairments, very little is known about the aetiology of autism. In the absence of an established pathogenesis for autism, medical clinicians and researchers have proposed explanations and subsequent treatments that involve regulation of diet and nutrition. One such diet that has received extraordinary attention is the casein-gluten restricted diet.

Introduction to the Casein-Gluten Restricted Diet

Strong advocates of the casein-gluten restricted diet argue that autism is the consequence of the incomplete breakdown and excessive absorption of peptides that are capable of affecting the endogenous opioid system (Reichelt et al., 1990). This hypothesis, often referred to as the exorphin theory of autism, originated as a result of observed similarities between the symptoms of autism and the long-term effects of morphine (Panksepp, 1979). It follows that the peptides produced through the digestion of dairy (casein) and wheat (gluten) are subject to incomplete breakdown in individuals with autism. These peptides have been labeled exorphins (which means exogenous morphine) to describe both their external origin from the food products as well as their resemblance to endorphins. This results in the formation of pre-opioid compounds capable of entering the bloodstream. The exorphin, Beta-casomorphin-7 (B-CM7), a peptide produced through the digestion of casein in milk, has received the most attention as the principal promoter of the symptoms of autism.

Studies have established that B-CM7 is capable of crossing the blood brain barrier - mediated, at least in part, by opioid receptors - readily activating brain cells in many areas theorized to be involved in autism (Sun et al., 1999a). Further research, involving the injection of B-CM7 into rats in order to observe behavioural responses, has yielded astonishing results. It was reported that roughly seven minutes after the injection of B-CM7 the rats became inactive, “distancing

Figure 1
Damage to the tight junctions linking intestinal epithelial cells causes increased absorption of harmful exorphins, such as B-CM7, through the mucosal barrier of the gut into the bloodstream.
themselves from the other rats in the same cage", while showing no social interaction and very little reaction to sound (Sun et al., 1999b). These B-CM7 induced behaviours exhibit a distinct resemblance to those observed in humans with autism.

**Intestinal Abnormalities**

It has been speculated that the incomplete breakdown of casein and gluten is the result of multiple intestinal abnormalities.

**Attenuated Genes**

The first abnormality, present in autistics, was observed to be the result of an attenuated enzyme, dipeptidyl peptidase-IV (DPPIV), thought to be involved in the digestion process (Brudnak, 2001). DPPIV is typically found in the enterocytes of the intestinal tract where it is involved in the degradation of casein and gluten residues. According to the exorphin theory of autism, the down-regulated levels of DPPIV could manifest as autistic symptoms.

**Increased Absorption**

The aforementioned catabolic deficiency is further intensified by what is referred to as the "leaky gut" nature of autism. As the title implies, individuals with autism have been found to experience unusually high levels of peptide absorption through the lumen of the gut. Past research has speculated towards the nature of this abnormal permeability, suggesting that this condition is the consequence of damage to the tight junctions linking the intestinal epithelial cells (D’Eufemia et al., 1996). These inadequate junctions allow for the increased absorption of harmful exorphins, such as B-CM7, through the mucosal barrier of the gut into the bloodstream (Fig. 1).

**Genomeceuticals: A Potential Alternative to the Diet**

The casein-gluten restricted diet has received extensive assessment from the scientific community since the discovery of its possible effectiveness by Reichelt and colleagues (1990). Despite the continual efforts of researchers to develop this treatment, its ability to successfully treat the symptoms of autism is based on parent testimonials, rather than clinical experimentation. In fact, it has been demonstrated that trying to completely eliminate all contributions of exorphins via the diet is neither practical nor 100% guaranteed (Brunak, 2001).

Although the casein-gluten restricted diet has been shown to yield promising results, inconsistencies in the treatment have led researchers and clinicians to explore alternate methods. This has allowed for the development of various enzyme and genomeceutical based treatments, both of which build upon the fundamental framework laid out by the casein-gluten restricted diet. Rather than prevent the ingestion of casein and gluten products as in the diet, enzyme and genomeceutical treatments focus on correcting the dysfunctional metabolism that is the source of the harmful exorphins through the use of enzymes and gene promoters.

Genomeceuticals describe naturally occurring nutrients that can affect (i) the structure of a gene, (ii) how well the transcribed products work and/or (iii) how much of it is made (Brunak et al., 2001). As previously stated, according to the exorphin theory of autism, the symptoms of autism may manifest due to the attenuated levels of dipeptidyl peptidase-IV (DPPIV) in the lumen. The genomeceutical model attempts to replenish the DPPIV levels through the use of enzyme promoters.

In recent research aimed towards alleviating the symptoms of autism, galactose has demonstrated the potential to serve as a genomeceutical. This potential surfaced from the observation that galactose increases the expression of DPPIV in murine enterocytes (Smith et al., 1991). The increased expression of DPPIV in the gastrointestinal tract could mend the dysfunctional digestion of casein and gluten in autistics. In addition to this, galactose is capable of stimulating the growth of probiotic organisms. This is of extraordinary importance, as probiotics are major contributors to the metabolic activity – including digestion – of their human host.

**Concluding Remarks**

Genomeceuticals have been used in conjunction with various enzyme-based treatments, but have yet to be used on their own. Research has established that the application of galactose as a genomeceutical increases the expression of an enzyme thought to be involved in the digestion of casein and gluten (DPPIV). This same enzyme has been found to be attenuated in autistics and, according to the exorphin theory of autism, is the principle promoter of the symptoms of autism. Although galactose has arisen as a prime candidate in the suppression of autistic symptoms, it still remains to be seen whether the application of genomeceuticals will be successful in clinical trials.