Intrinsic Factor

Vitamin B12 or cobalamin is an essential coenzyme that needs to be taken up with the diet (O'Leary and Samman 2010). One enzyme requiring cobalamin as coenzyme is methionine-synthase, which is involved in the regeneration of tetrahydrofolate for the *de novo* synthesis of purine and pyrimidine bases. Therefore, a lack of cobalamin can cause anemia by negatively affecting the cell proliferation activity of the bone marrow and in turn the production of erythrocytes (O'Leary and Samman 2010; Rush *et al*. 2014). Another enzyme requiring cobalamin as coenzyme is methylmalonyl-CoA mutase. This enzyme catalyzes the conversion of methylmalonyl-CoA to succinyl-CoA to fuel the citric acid cycle, and it is believed that the accumulation of methylmalonyl-CoA causes the neurological defects associated with cobalamin deficiency (O'Leary and Samman 2010; Rush *et al*. 2014).

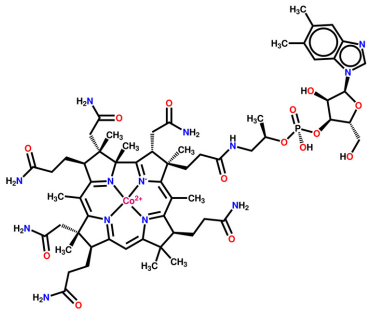


Figure 1: Model structure of vitamin B12 (cobalamin).

Absorption of cobalamin requires intrinsic factor, a glycoprotein that is secreted by parietal cells and forms a complex with cobalamin in the duodenum. In the distal part of the ileum, this complex is endocytosed by binding to the mucosal cell receptor cubilin. Following its release from intrinsic factor, cobalamin is bound by transport proteins called transcobalamins and distributed throughout the body via the blood system (O'Leary and Samman 2010; Andrès *et al*. 2004).

Pernicious anemia, first described by Thomas Addison in 1849, is an autoimmune disease that affects approximately 15 – 20% of elderly patients suffering from cobalamin deficiency (Andrès *et al*. 2004; Annibale *et al*. 2011). Besides atrophic gastritis, inflammation and destruction of the gastric mucosa, autoantibodies against intrinsic factor have been reported to be highly specific for and to be detected in approximately 50 – 60% of the patients diagnosed with pernicious anemia (Taylor 1959; Andrès *et al*. 2004; Bizzaro and Antico 2014; Schade *et al*. 1967a; Schade *et al*. 1967b). Two types of anti-intrinsic factor autoantibodies that bind to different epitopes are known. While type I antibodies block the formation of the intrinsic factor-cobalamin complex, type II antibodies inhibit the binding of the complex to its receptor in the ileum (Schade *et al*. 1967a; Schade *et al*. 1967b). Using recombinant intrinsic factor, both types of antibodies could be detected in patient samples (Nexo *et al*. 2005).

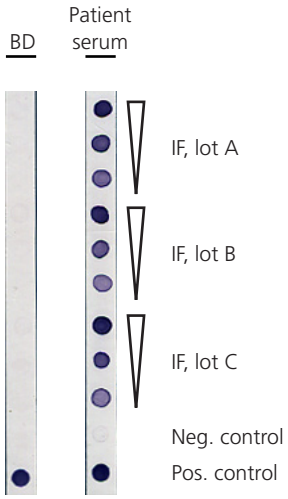


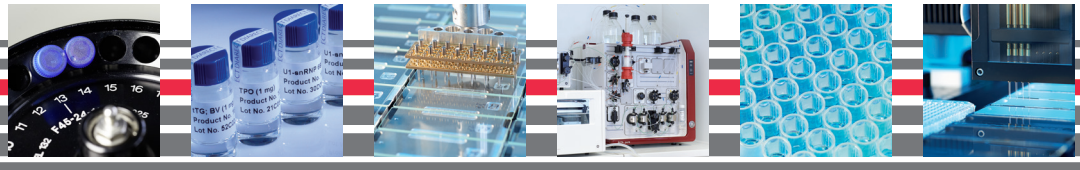
Figure 2: Immunodot analysis of increasing amounts of three different lots of recombinant intrinsic factor (IF) using a serum from a blood donor (BD) and a patient with presumed pernicious anemia.

DIARECT's recombinant full-length intrinsic factor is produced in the baculovirus/insect cell expression system.

Ordering Information		
16700	Intrinsic Factor	0.1 mg
16701		1.0 mg

References:
Addison (1849) London Med Gazette. 43:517-518
Andrès *et al*. (2004) CMAJ. 171:251-259
Annibale *et al*. (2011) Curr Gastroenterol Rep. 13:518-524
Bizzaro and Antico (2014) Autoimmun Rev. 13:565-568
Nexo *et al*. (2005) Clin Chem Lab Med. 43:351-356
O'Leary and Samman (2010) Nutrients. 2:299-316
Rush *et al*. (2014) Eur J Clin Nutr. 68:2-7
Schade *et al*. (1967a) J Clin Invest. 46:615-620
Schade *et al*. (1967b) Clin Exp Immunol. 2:399-413
Taylor (1959) Lancet. 274:106-108

210416_Rev04



DIARECT GmbH · Bötzinger Str. 29 B · 79111 Freiburg · Germany
Tel. +49 (0) 761 47979-0 · Fax +49 (0) 761 47979-29 · orders-dia@bbisolutions.com · www.bbisolutions.com