Protein S

General:

Protein S is a cofactor of protein C and is also vitamin K dependent. Protein S circulates in plasma usually linked to C4b-binding protein to 60%. Approx. 40% are present as free protein S with co-factor function. Activated protein S can be inhibited by two plasma proteins, protein C-inhibitor and α1-antitrypsin. Protein S supports the binding between protein C and the phospholipid surface membrane and enhances the reaction of APC with factors V and VIII by factor 30. The first screening test for Protein S detects the biological functionality (activity) of protein S. In case of a Protein S deficiency total and free Protein S should be tested for pre-classification.

Protein S deficiency is a disorder associated with increased risk of venous thrombosis. Protein S, a vitamin K dependent physiological anticoagulant, acts as a nonenzymatic cofactor to activated protein C in the proteolytic degradation of factor Va and factor VIIIa. Decreased (antigen) levels or impaired function (activity) of protein S lead to decreased degradation of factor Va and factor VIIIa and an increased propensity to venous thrombosis. Protein S circulates in human plasma in two forms: approximately 60 percent is bound to complement component C4b β-chain while the remaining 40 percent are free. Only free protein S has activated protein C cofactor activity.

There are three types of hereditary protein S deficiency:

Type I – decreased protein S activity: decreased total protein S (=both bound and free protein S) levels and decreased free protein S levels (quantitative defect)

Type II – decreased protein S activity: normal free protein S levels and decreased total protein S levels (qualitative defect)

Type III – decreased protein S activity: decreased free protein S levels and normal total protein S levels (quantitative defect)

Protein S deficiency can also be acquired due to vitamin K deficiency or treatment with warfarin, systemic sex hormone therapy and pregnancy, liver disease, and certain chronic infections (for example HIV). Vitamin K deficiency or treatment with warfarin generally also impair the coagulation system itself (factors II, VII, IX and X), and therefore predispose to bleeding rather than thrombosis. Protein S deficiency is the underlying cause of a small proportion of cases of disseminated intravascular coagulation (DIC), deep venous thrombosis (DVT) and pulmonary embolism (PE).

The following tests are available:

- **Protein S activity**

  Indication: Risk assessment of thrombosis, unclear thromboembolism

  Material: 2 ml citrate blood

  Preanalytics: citrate plasma: 1 part citrate + 9 parts blood. Frozen plasma! Plasma supernatant must be dispatched frozen!

  TAT: 7-10 days*

  Method: COAG

  Units: %

  Ref.- range: see report

  Note: The examinations should be carried out approx. 2 weeks after stopping coumarin/ warfarin therapy. Please note that the factor V mutation as well as the factor II mutation are the most common causes in familial thrombophilia.

- **Protein S antigen, free**

  Indication: Classification of protein S deficiency

  Material: 3 ml citrate blood

  Preanalytics: citrate plasma: 1 part citrate + 9 parts blood, frozen plasma! Plasma supernatant must be dispatched frozen!

  TAT: 7-10 days*

  Method: TURB

  Units: %

  Ref.- range: see report

- **Protein S antigen, total**

  Indication: Classification of protein S deficiency

  Material: 3 ml citrate plasma frozen

  TAT: 7-10 days*

  Units: %

  Ref.- range: 60 – 150

For complete list of laboratory test offered at Freiburg Medical Laboratory, please visit http://www.fml-dubai.com/parameter-listings/