Elecsys® ProGRP

Electro-chemiluminescence immunoassay (ECLIA) for the quantitative determination of human progastrin-releasing peptide (ProGRP) in serum and plasma

Indication

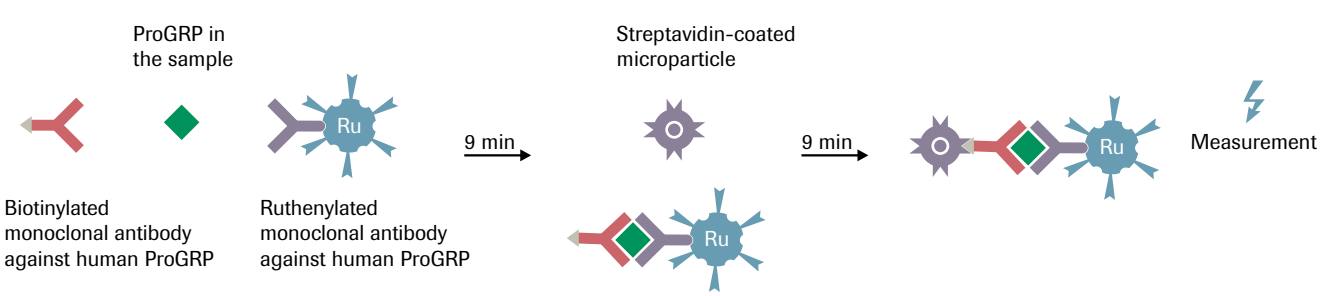
The assay is used to aid in the differential diagnosis in lung cancer. It is important to distinguish between the two main histological types of the disease, small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), as they have have different treatments and prognoses.

ProGRP is the precursor of gastrin-releasing peptide (GRP). GRP is an important regulatory molecule that has been implicated in a number of physiological and pathophysiological processes in humans. GRPs are also thought to be produced by cells of SCLC where they act in the metastatic process via their autocrine activity or through cell-to-cell interactions. Due to its short half-life of 2 minutes. it is difficult to determine GRP in blood. Therefore, ProGRP which has a longer half-life in blood can be measured by immunoassays.

ProGRP is the marker of choice for SCLC

- ProGRP is related with the histological subtype in lung cancer. It has been reported as a specific tumor marker for SCLC and neuroendocrine carcinomas.[1,2] Abnormal levels may be found in a small subset of patients without SCLC, but these concentrations are significantly lower than the ProGRP serum levels found in SCLC patients.[3] Similar results have been reported with neuron-specific enolase (NSE).[4]
- ProGRP even has a high sensitivity in the early stages of the disease, which is greater than that of NSE. Sensitivity can be further enhanced by the combined use of ProGRP and NSE.[5]
- ProGRP serum levels serve as a predictor of relapse of SCLC [6] and are related to tumor extension. Serum levels > 150 pg/mL are indicative of SCLC with a probability of 93 %.[7]

Test principle: one-step sandwich assay



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Life needs answers

Elecsys® technology

ECL (ElectroChemiLuminescence) is Roche's technology for immunoassay detection. Based on this technology and combined with well-designed, specific and sensitive immunoassays, Elecsys delivers reliable results. The development of ECL immunoassays is based on the use of a ruthenium-complex and tripropylamine (TPA). The chemiluminescence reaction for the detection of the reaction complex is initiated by applying a voltage to the sample solution resulting in a precisely controlled reaction. ECL technology can accommodate many immunoassay principles while providing superior performance.

Elecsys® ProGRP assay characteristics:	
Testing time	18 min.
Test principle	One-step sandwich assay
Calibration	2 point calibration
Traceability	Abbott ARCHITECT ProGRP
Sample material	• Serum collected using standard sampling tubes or tubes containing separating gel • Li-heparin plasma, K_2-EDTA and K_3-EDTA plasma
Sample volume	30 µL
Limit of detection (LoD)	3 pg/mL
Measuring range (lower end defined by LoD)	3 – 5,000 pg/mL
Intermediate imprecision (measured with human plasma samples and PreciControl ProGRP)	**cobas e** 411 analyzer, E2010: 2.1 – 4.2 % **cobas e** 601 / **e** 602 modules, E170: 3.0 – 6.8 %
Repeatability (measured with human plasma samples and PreciControl ProGRP)	**cobas e** 411 analyzer, E2010: 0.7 – 2.6 % **cobas e** 601 / **e** 602 modules, E170: 0.8 – 3.7 %
Limit of quantitation (LoQ) (defined at total error of ≤ 30%)	Designed to have a LoQ of 7 pg/mL. For LoQ 3 human plasma samples were diluted and measured in 6 runs over 3 days on 2 analyzers. At a total allowable error of ≤ 30 % the LoQ was 3.99 pg/mL

Expected values

A study in Germany with the Elecsys® ProGRP assay on 698 samples from apparently healthy caucasian adults (336 males, 362 females) aged between 18 and 79 years yielded the following results:[8]

	ProGRP (pg/mL)			
	5th percentile (C.I.)	**Median (C.I.)**	**95th percentile (C.I.)**	**97.5th percentile (C.I.)**
Serum	25.3	40.3	69.2 (63.8 – 75.3)	77.8 (74.6 – 99.6)
Li-Heparin plasma	25.7	41.4	68.0 (63.7 – 74.5)	77.0 (73.0 – 101.1)
EDTA plasma	22.2	35.5	59.5 (55.8 – 65.3)	68.1 (64.1 – 84.9)

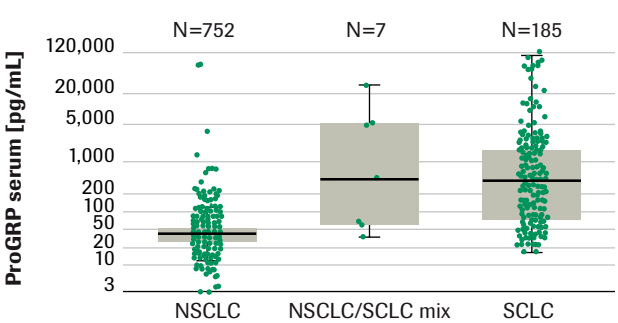
C.I. = confidence interval

The distribution of ProGRP values determined by 4 centers in Europe using the Elecsys® ProGRP assay for 2,163 serum specimens is summarized in the table below:

		Elecsys® ProGRP values (pg/mL)				
		< 3.0	3.0 - 50	50 – 100	100 – 200	> 200
	N total	N (Percentage distribution)				
Apparently healthy						
Smokers	174	0 (0)	140 (80.5)	34 (19.5)	0 (0)	0 (0)
Past smokers	61	0 (0)	46 (75.4)	15 (24.6)	0 (0)	0 (0)
Non smokers	463	0 (0)	347 (74.9)	108 (23.3)	8 (1.7)	0 (0)
Benign conditions*						
Benign lung diseases	35	0 (0)	31 (88.6)	4 (11.4)	0 (0)	0 (0)
Renal diseases	29	0 (0)	4 (13.8)	6 (20.7)	13 (44.8)	6 (20.7)
Other benign diseases	120	0 (0)	100 (83.3)	20 (16.7)	0 (0)	0 (0)
Cancer						
SCLC	185	0 (0)	33 (17.8)	24 (13.0)	17 (9.2)	111 (60.0)
NSCLC	752	0 (0)	543 (72.2)	182 (24.2)	14 (1.9)	13 (1.7)
NSCLC/SCLC mix	7	0 (0)	1 (14.3)	2 (28.6	0 (0)	4 (57.1)
Mesothelioma	27	0 (0)	24 (88.9)	3 (11.1)	0 (0)	0 (0)
Thyroid medullary	15	0 (0)	2 (13.8)	1 (6.7)	0 (0)	12 (80.0)
Neuroendocrine carcinoma	23	0 (0)	10 (43.5)	6 (26.1)	2 (8.7)	5 (21.7)
Breast	53	0 (0)	40 (75.5)	12 (22.6)	0 (0)	1 (1.9)
Ovarian	36	0 (0)	25 (69.4)	8 (22.2)	2 (5.6)	1 (2.8)
Prostate	32	0 (0)	18 (56.3)	9 (28.1)	5 (15.6)	0 (0)
Colorectal	61	0 (0)	43 (70.5)	15 (24.6)	3 (4.9)	0 (0)
Other malignancies	90	0 (0)	67 (74.4)	18 (20.0)	5 (5.6)	0 (0)

Use of ProGRP for the primary differential diagnosis in lung cancer

The differentiation ability of ProGRP regarding SCLC vs. NSCLC was investigated in a study on 944 patients, (185 SCLCs, 752 NSCLCs and 7 NSCLC/SCLC mix) and ProGRP levels were correlated with histology. The distribution of values is shown in the box-plot and the 2x2 table below:



	NSCLC	SCLC	N
ProGRP ≤ 85.7 pg/mL	714	51	765
ProGRP > 85.7 pg/mL	38	134	172
N	752	185	937

The cut-off value for a specificity of 95% (based on NSCLC collective) was 85.7 pg/mL.

The correlation of Elecsys® ProGRP values and stage for 168 patients with SCLC.

	N	5th percentile (pg/mL)	Mean ProGRP (pg/mL)	Median ProGRP (pg/mL)	95th percentile (pg/mL)
Stage I-II SCLC	11	17.9	232.6	75.9	781.1
Stage III SCLC	57	28.4	2718.4	300.8	2985.0
Stage IV SCLC	100	32.5	5181.9	585.3	21830.0
NSCLC Stage I-IV	752	15.8	135.4	38.6	85.7
SCLC/ NSCLC mix	7	33.5	5046.5	416.0	25240.0
Benign lung disease	35	14.0	32.8	32.6	54.8

Order information

Elecsys® ProGRP	100 tests	06505961 190
Elecsys® ProGRP CalSet	4 x 1 mL	06505970 190
PreciControl ProGRP	2 x 1 mL each	06505988 190
Diluent MultiAssay	2 x 16 mL sample diluent	03609987 190

References

1 Miyake, Y., Kodama, T., Yamaguchi, K. (1994). Pro-gastrin-releasing peptide(31–98) is a specific tumor marker in patients with small cell lung carcinoma. *Cancer Res. 54,* 2136–2140.

2 Molina, R. (2009). ProGRP: A New Biomarker for Small Cell Lung Cancer. *EJCMO. 1,* 25-32.

3 Stieber, P., Dienemann, H., Schalhorn, A., et al. (1999). Pro-gastrin-releasing peptide (ProGRP)—a useful marker in small cell lung carcinomas. *Anticancer Res. 19,* 2673–2678.

4 Niho, S., Nishiwaki, Y., Goto, K., et al. (2000). Significance of serum pro-gastrin-releasing peptide as a predictor of relapse of small cell lung cancer: comparative evaluation with neuron-specific enolase and carcinoembryonic antigen. *Lung Cancer. 27,* 159–167.

5 Shibayama, T., Ueoka, H., NishiiI, K., et al. (2001). Complementary roles of pro-gastrin-releasing peptide (ProGRP) and neuron specific enolase (NSE) in diagnosis and prognosis of small cell lung cancer (SCLC). *Lung cancer. 32,* 61 – 69.

6 Niho, S., Nishiwaki, Y., Goto, K., et al. (2000). Significance of serum progastrin-releasing peptide as a predictor of relapse of small cell lung cancer: comparative evaluation with neuron-specific enolase and carcinoembryonic antigen. *Lung Cancer.* 27, 159–167.

7 Molina, R., Auge, J.M., Bosch, X., et al. (2009). Usefulness of serum tumor markers, including progastrin-releasing peptide in patients with lung cancer: correlation with histology. *Tumor Biol. 30,* 121–129.

8 Roche study No. RD001525 and RD000788.

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