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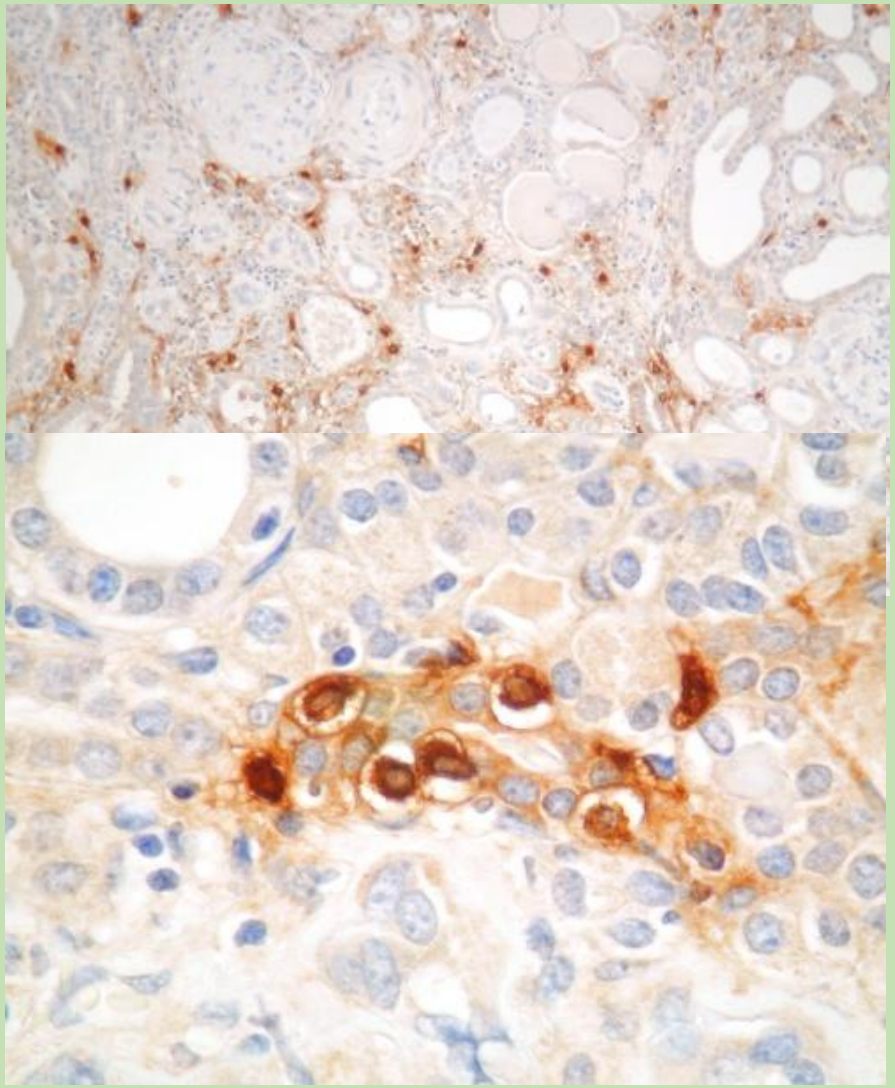
TRYPTASE AS A NOVEL MARKER FOR AML AND CML PATIENTS



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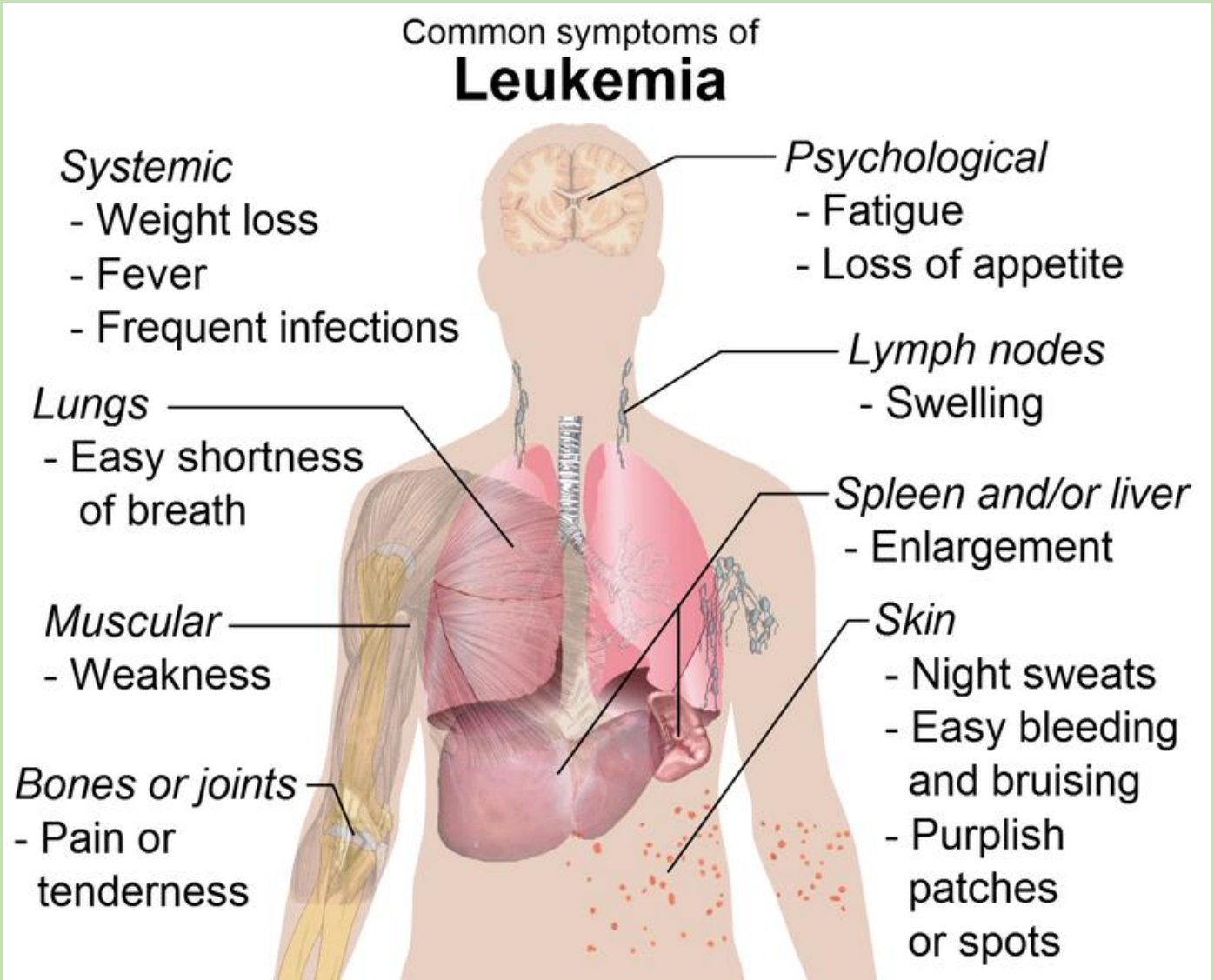
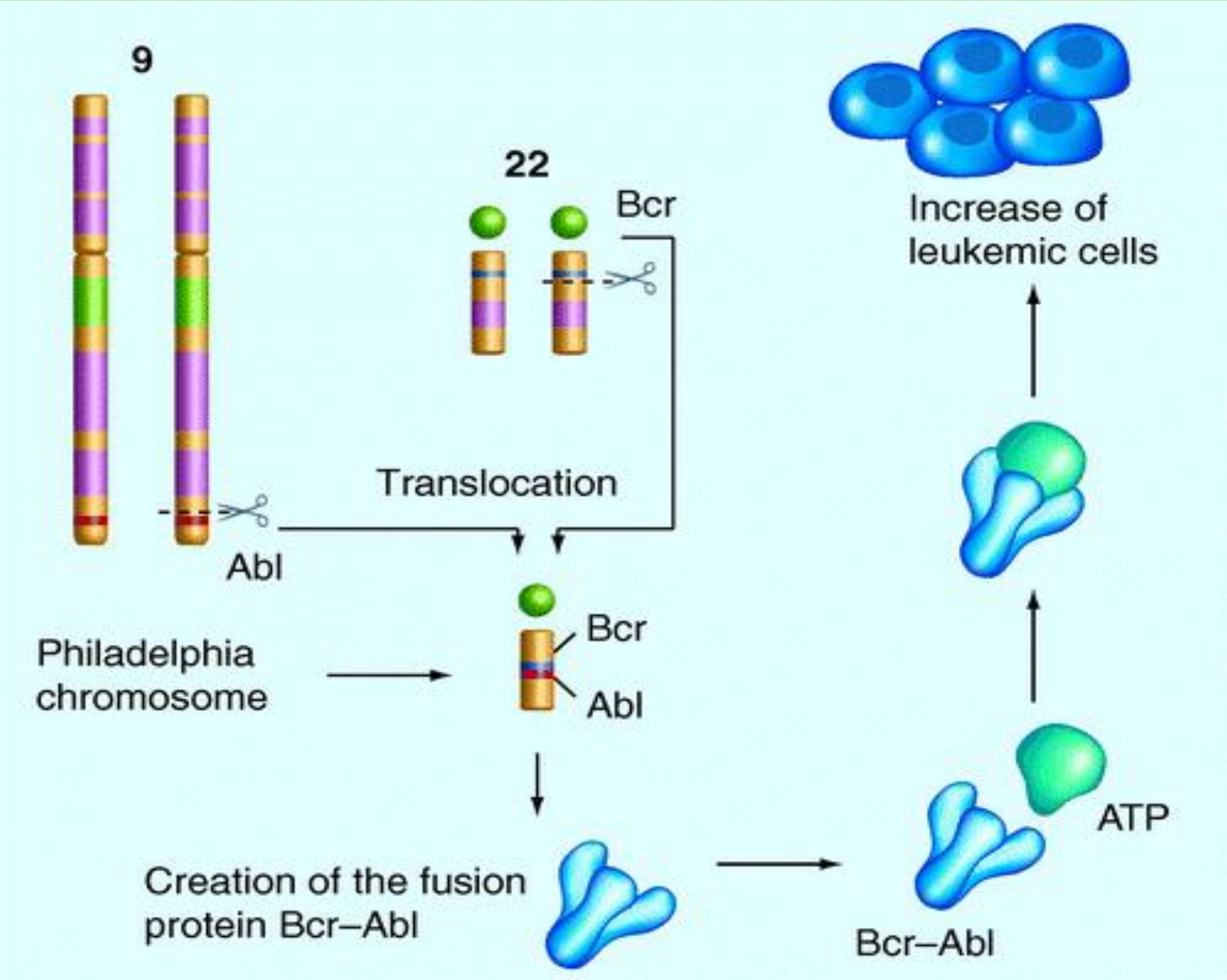
Leukemia

- Neoplastic proliferative disorders of bone marrow or blood cells
- Types: Myeloid and Lymphoid
- Both can be acute or chronic



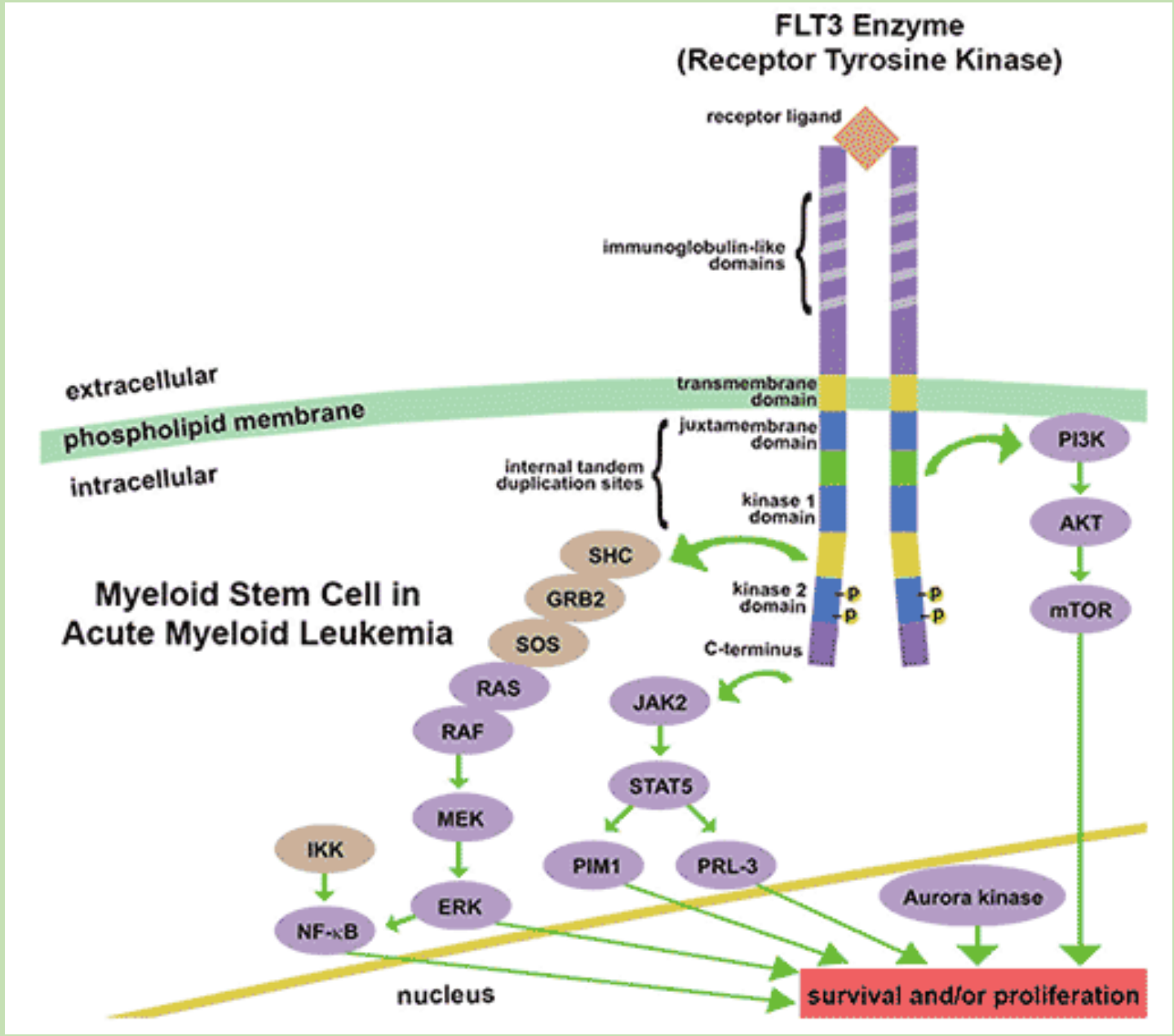
Bcr-abl in leukemia

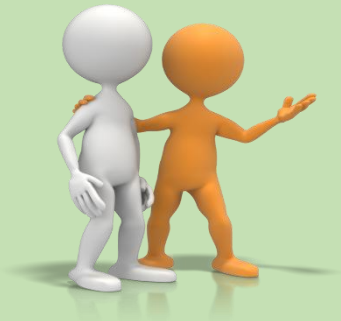


Common pathogenic feature

- Mutated
- Constitutively activated

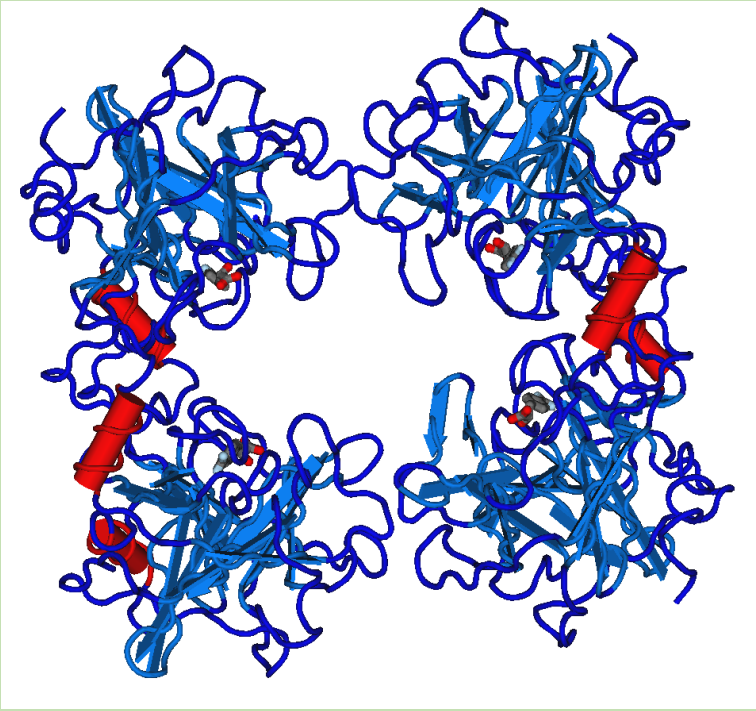
Tyrosine kinase

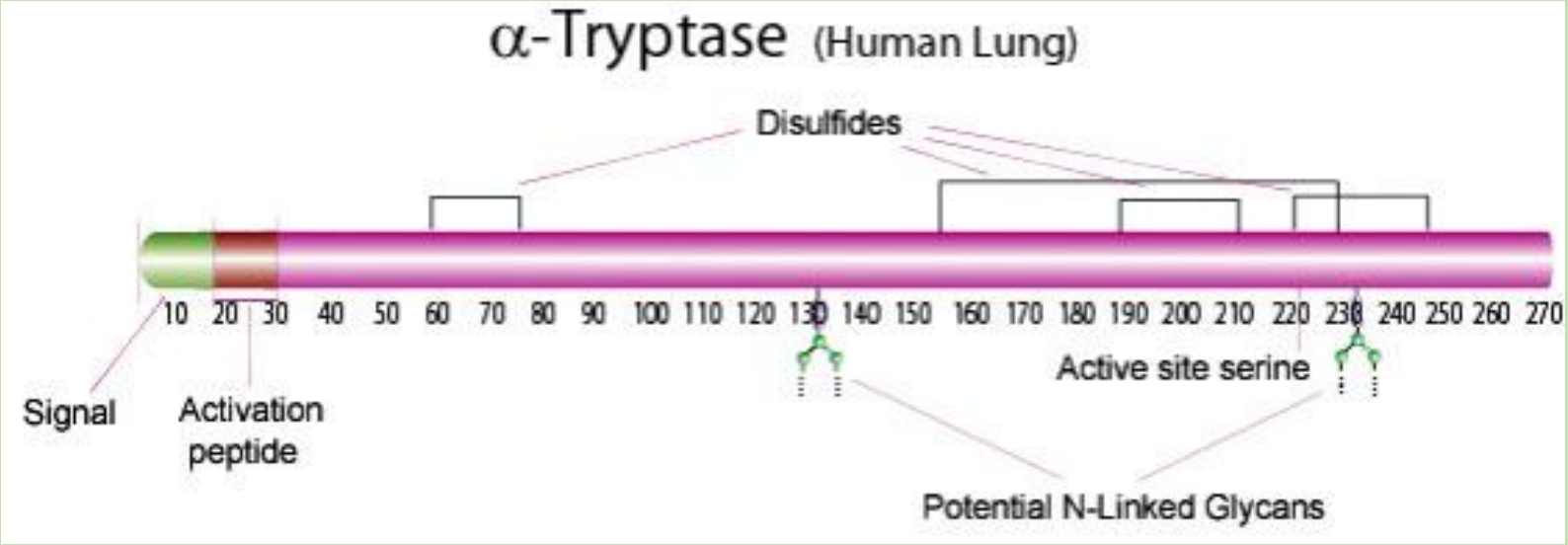




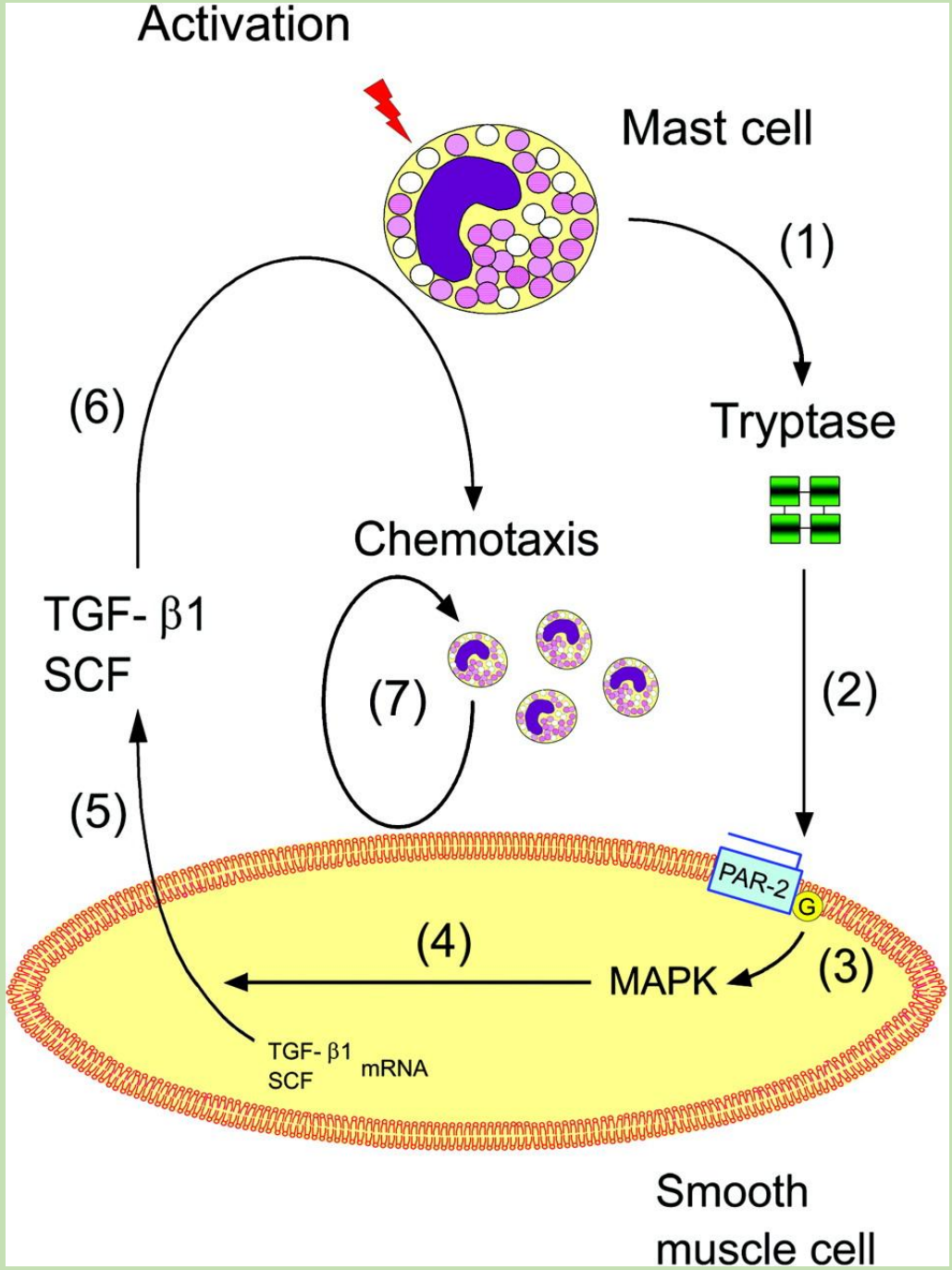
Tryptase

- Serine protease expressed in mast cells
- Marker of mast cell activation
- α β and δ genes and alleles have been identified





Tryptase AND MAST CELLS



Elevated total Tryptase:

- Acute Myelocytic leukemia
- Myelodysplastic syndrome
- Hypereosinophilic syndrome

Tryptase is expressed in

- Myeloblasts in AML
- Basophils in CML

- Tryptase estimation in CML & AML : prognostic significance

Aims & Objectives

- To evaluate & compare the levels of serum Tryptase in patients of AML& CML before and after treatment

- To evaluate & compare the levels of serum Tryptase in patients of AML& CML with controls

Material and Method

- 20 AML patients
- 20 CML patients
- 40 age & sex matched healthy controls

- Diagnosis: TLC, DLC, Bone marrow, cytogenetics

CR INDUCTION REGIMES

- Cytarabine and Anthracycline
- Cytarabine is usually administered as a continuous intravenous infusion for 7 days.
- Anthracycline therapy generally consists of daunorubicin intravenously on days 1, 2, and 3 (the 7 and 3 regimen).
- After induction chemotherapy, if persistence of leukemia is documented, the patient is usually re-treated with cytarabine and an anthracycline in doses similar to those given initially, but for 5 and 2 days, respectively.

Sample collection

- 5 ml venous blood was collected:
- At the time of diagnosis
- After 3 months of treatment
- Healthy controls

- Serum Tryptase analyzed by kit based on double-antibody sandwich enzyme-linked immunosorbent assay (ELISA) to assay the level of Human Mast Cell Tryptase (MCT) in samples

Results and observations

	Parameter	AML	CML
1.	Mean age	58.4±15.73 years	51.4±13.27 years
2.	Male to female ratio	1.5: 1	1.8: 1
3.	Mean Hb (g/dl)	8.17g/dl	10.3g/dl
4.	Total leukocyte count	16530/mm^3	152650/mm^3
5.	Platelets	78525/mm^3	4.2 lakhs/mm^3

- TABLES no 1. Mean values of cases of AML and CML

Results and observations continued…

s. no	Parameter	AML	CML
1.	Mean value of % peripheral blasts at diagnosis	5.79±19.65	7.95±5.90
2.	Mean value of % peripheral blasts after chemotherapy	5.9±14.36	1.45±4.35
3.	Reduction in % of peripheral blasts significance, p value	< 0.001	<0.005
4.	Serum tryptase before chemotherapy (cases)	19.3±9.04ng/dl	17.22±8.64ng/dl
5.	Serum tryptase (controls)	5.32±2.84ng/dl	5.15±2.66ng/dl
6.	Difference between cases and controls, p value	<0.000	<0.000
7.	Difference between cases before and after chemotherapy, p value	<0.003	<0.017

- TABLE no 2. Percentage of Blasts and Serum Tryptase in AML and CML

Results and observations continued…

	AML		CML	
	Normal tryptase levels (<15ng/dl)	Elevated tryptase levels (>15ng/dl)	Normal tryptase levels (<15ng/dl)	Elevated tryptase levels (>15ng/dl)
Number of cases	12	8	13	7
Percentage of blasts	44.16±11.47	78.50±9.41	3.76±1.23	15.71±2.21

TABLE no 3 SERUM TRYPTASE LEVELS AND BLASTS %

- **It has been observed :**

- Increased serum Tryptase in patients of AML & CML at the time of diagnosis
- Significant decrease after complete remission

- All CML cases in present study was Philadelphia chromosome positive.

- Imatinib binds at ATP binding site of BCR/ABL resulting in “switching off” the signalling pathway which promote abnormal growth

DISCUSSION

- Recent studies have shown that a number of myeloid leukemia cell lines also express substantial amounts of tryptases.

- In present study out of 20 AML & 20 CML patients 8 & 7 were showing raised (>15ng/dl) levels respectively

- Sperr et al done study on AML patients and reported that in these patients serum tryptase level were elevated and reflect the total burden of leukemic cells.

- Our data showed that levels of tryptase were elevated at the time of diagnosis in 40 percent patients of AML and 35 percent patients of CML

- After chemotherapy 80 percent patients of AML and 90 percent patients of CML achieved complete remission and levels of serum tryptase were significantly reduced after chemotherapy in patients who achieved remission.

- Similar significant reduction in percentage of blast cells were observed in patients who achieved remission after chemotherapy.

- Significant decrease in serum tryptase levels were seen during induction treatment, and at the time of complete remission in the majority of the patients parameters returned to normal limits, whereas blast cell persistence was associated with a persistently elevated enzyme level

- Similar finding were reported in various studies by Puchit, Kiener, Schwartz, Jordan and Sperr in myeloid leukemia. They found that s.tryptase levels were elevated in patients of AML and CML at the time of diagnosis

- Sperr et al reported that under physiological condition myeloid cells (except mast) are virtually tyrptase negative

Conclusion

- Tryptase may be useful for diagnosis, assessment of severity of disease (leukemic cell burden), monitoring minimal residual disease and prognosis of both AML and CML patients.

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