

# Clinical utility and safety of *Ganoderma lucidum* (Bio-Ganoderma) in Acute Lymphoblastic Leukaemia as a adjuvant therapy: a case report

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## INTRODUCTION

### Leukaemia

- Acute Lymphoblastic Leukaemia (ALL) is the most common childhood malignancy in developed countries (annually about 3/5 cases per 100.000 children).
- Optimal utilisation of antileukemic drugs in addition with supportive care achieves highest survival rates (about 85 %) for children diagnosed at 1-4 years.

### Chemotherapy

- The main side effects are caused by drug toxicity and include myelosuppression, mucositis, nausea and vomiting among survivors, as well as recurrent infections.
- Patients with cancer have altered pharmacokinetics and complex clinical conditions that require complex drug regimens.

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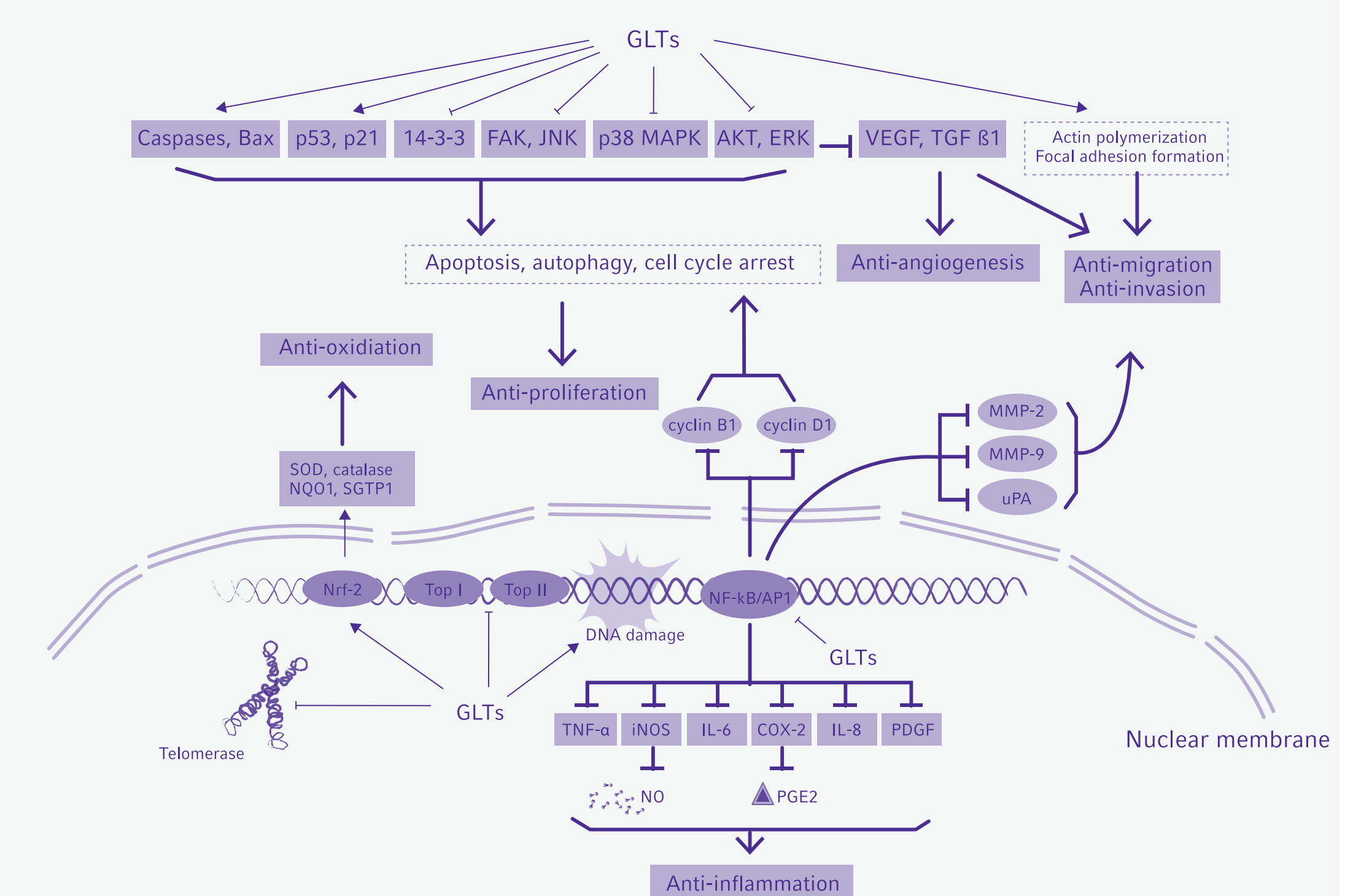
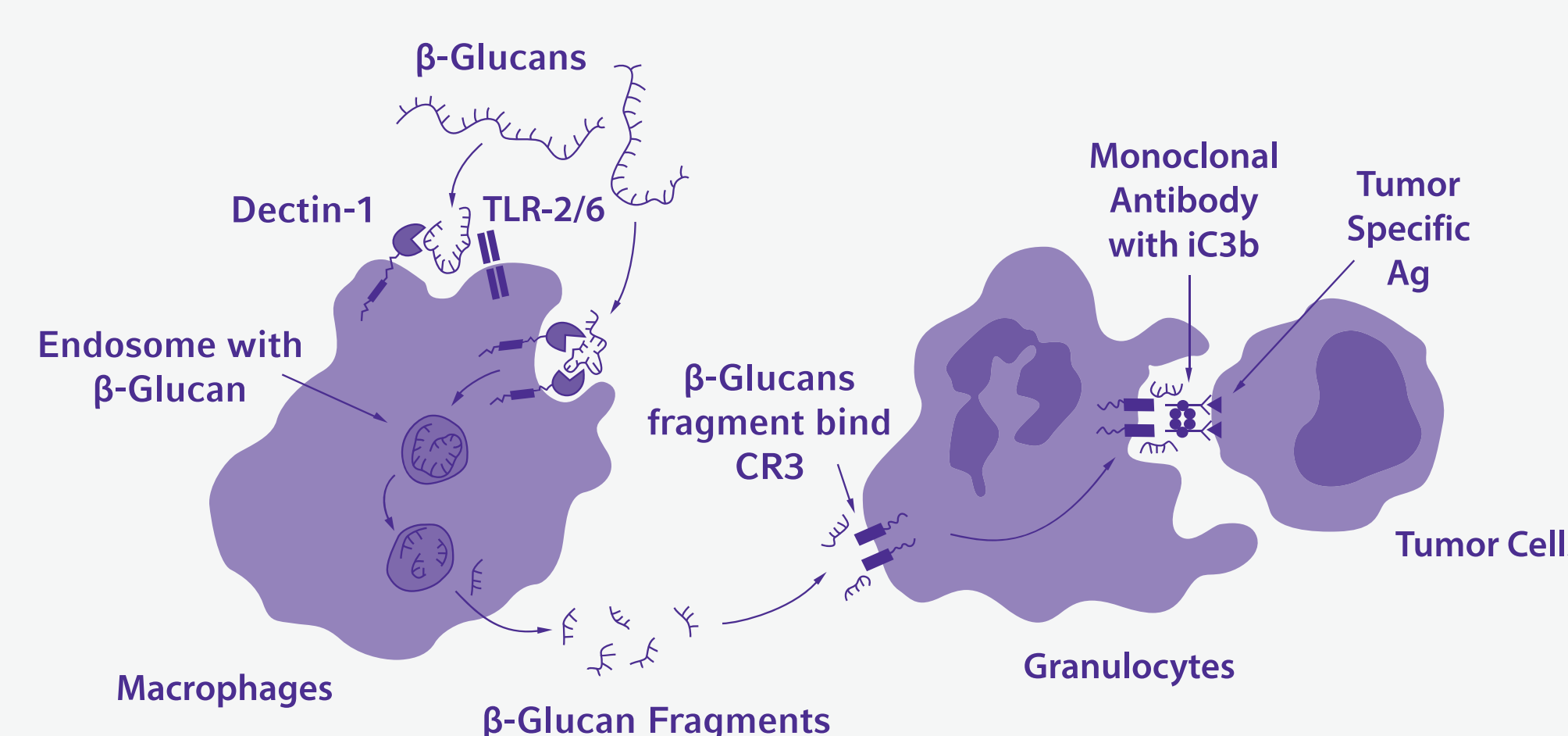
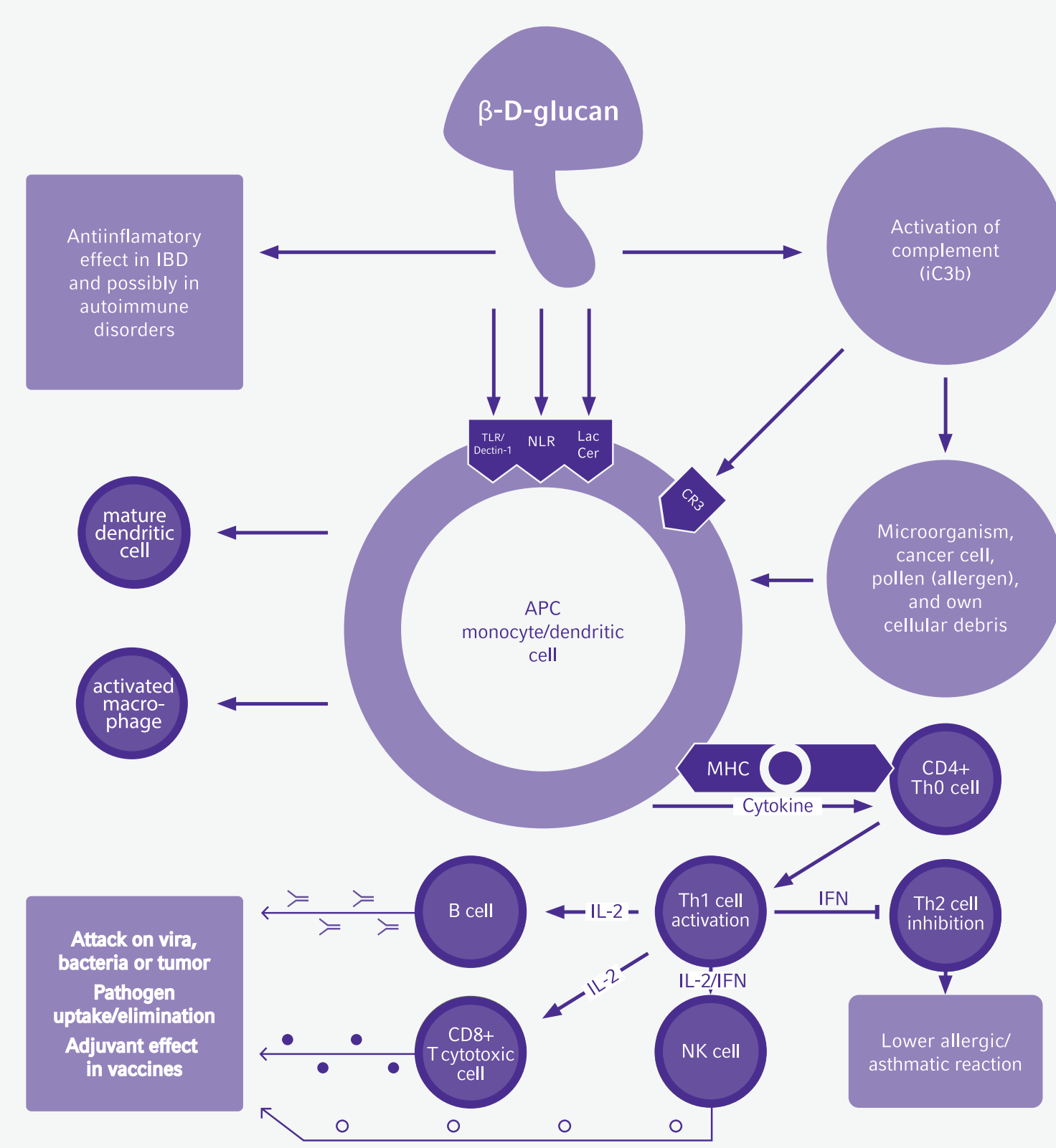
- Complementary Medicines are often used in Paediatric Oncology.
- Medicinal mushrooms are Biological Response Modifiers (BRM), improving the ability of the immune system to fight infections, cancer and other diseases.
- The medicinal mushroom *Ganoderma lucidum* (Reishi) has a long record of safe use and has been extensively targeted in research studies globally.

*Ganoderma lucidum* can work as adjuvant to chemotherapy in oncology patients:



- It can exert a direct antitumour activity on cancer cells and also it can enhance the sensitivity of these cells to chemotherapeutic agents such as Cisplatin (Zhao *et al.*, 2011).
- Its polysaccharides inhibits migration of human cancer cells and also induce apoptosis on these cells (Liang *et al.*, 2015).
- It can work as hepatoprotective agent in chemically-induced toxicity, thus preventing liver injury (Wu *et al.*, 2013).
- It is able to suppress cancer metastasis through the inhibition of pro-invasive genes (Loganathan *et al.*, 2014).
- Its ergosterol peroxide helps to overcome chemoresistance on aggressive cancer cells that have acquired resistance to this therapeutic agents (Wu *et al.*, 2012).

## Mechanisms of action of mushrooms bioactive compounds in oncology



- $\beta$ -(1,3)(1,6)D-Glucans present in medicinal mushrooms modulate human immune system, playing a role in disease control. Membrane receptors found in the immune cells interact with B-D-Glucans activating signalling pathways involving innate and adaptive responses. Implications include allergy, cancer, pathogen elimination, inflammatory bowel disease and autoimmune disorders (Figure adapted from Hetland *et al.*, 2011).

- $\beta$ -D-Glucans are rapidly captured and taken up by macrophages in the proximal small intestine. Macrophages internalise and process these molecules, releasing them in the bone marrow and reticuloendothelial system. Circulating granulocytes recognize those processed B-D-glucans, activating multiple effector pathways (adapted from Chan *et al.*, 2009).

- Ganoderma lucidum* triterpenes are major anti-cancer compounds. These compounds target evasion of anti-growth signalling and sustaining proliferative signalling (MAPK/ERK, etc.), induce apoptosis and autophagy, suppress cell migration and invasion, inactivate telomerase and DNA topoisomerases, inhibit tumor-promoting inflammation and exert anti-angiogenic activity (Wu *et al.*, 2013).

## AIM OF ADJUVANT THERAPY

- To improve survival and quality of life, as well as prevent short and long term side effects in children receiving conventional treatments.
- To promote benefits, acting in different ways, such as:
  - Antimutagenic agent
  - Immunomodulator (polysaccharides)
  - Cytotoxic effect in tumoral cells
  - Anti-angiogenic (ergosterol)
  - Antioxidant (enzymes, vitamins, sterols, etc.)
  - Promotes cell differentiation in tumoral cells (arrest cycle, increases caspases, activate p53)
  - It is a natural immunotherapeutic
- It is a natural immunotherapeutic
- Ganoderma lucidum* previous showed to increases lymphoproliferative responses in immunocompromised children with cancers in a randomised, double blind and placebo controlled study.
- However, clinical evidence supporting the use of medicinal mushrooms (Reishi) in Paediatric patients is still scarce.

## CASE STUDY

- A 4 years old boy with confirmed diagnosis of ALL type B without leucocytosis. Initial parameters:
  - Ecchymosis, cutaneous pale, fever
  - Anemia (Hb 4.8 g/dL), Leucocytosis ( $74 \times 10^9/L$ ), Blasts 91 %, Thrombocytopenia ( $28 \times 10^9/L$ )
- The patient followed the Protocol 58081 of the EORTC with good response.
- He finished his chemotherapy treatment 2 years after the initial diagnose date, with a complete remission.
  - Chemotherapy treatment:**
    - Mercaptopurine + MTX
    - Vincristine + DMX
  - After getting the Informed Consent from their parents, and estimate the initial dose based on BW (mg/kg), the child start receiving an initial oral dose of 445 mg of Bio-Ganoderma daily with excellent tolerance.
    - Starting parameters:
      - Blood test normal: BWC  $10 \times 10^9$ , N 77.9 %, L 15 %
      - Myelogram normal
    - Excellence tolerance to the treatment allowed to increase the dose to 890 mg six months later, with again excellent clinical response as well as tolerability.
    - Two years later, daily providing the same oral dose, the patient still was free from infection, no recurrence of his malignancy (analytically confirmed) neither side effects.
      - Parameters after 6 months of Mycotherapy only:
        - Blood tests normal
        - Myelogram normal
      - Currently, the child is 7 years old, his BMI is within the corresponding percentiles, and his psychomotor development has been completely normal, performing the activities of a child of his age, both at the physical as intellectual level. Likewise, her parents report that he shows good appetite and mood, as well as normal family and school relations.

## CONCLUSIONS

- We need novel therapeutic approaches for Paediatric Cancer in order to improve the quality of life, prevent consequences and recurrences.
- Ganoderma lucidum* is a safe complement in Oncologic patients, due to:
  - It does not interact with chemotherapy (it does not interfere with cytochrome P450, it does not contain heavy metals, pesticides or toxic compound due to its organic origin, it does not contains plants or other substances that can interfere metabolic pathways of chemotherapy)
  - It does not have any contraindication, except people allergic to mushrooms
- Ganoderma lucidum* improves the performance status:
  - $\beta$ -D-Glucans enter the proximal small intestine and are rapidly captured by macrophages after oral administration. Processed  $\beta$ -D-Glucans are then transported to the reticuloendothelial system eliciting an immune response
  - It also improves nutritional status because of it contains a high amount of proteins, vitamins and minerals
- As for adults, *Ganoderma lucidum* is an excellent opportunity for paediatric patients due to its safety, tolerability and clinical response. It demonstrates in children:
  - Reduction of hospitalisation
  - Improving quality of live
  - Provide economic benefits for Health Public System

## IN SUMMARY

*Ganoderma lucidum* is a potent natural compound for Leukaemia therapy in children, safe and effective.

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