Advancing a Lipedema Research Roadmap: Recommendations to characterize the biology of a complex disease

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Introduction

- Lipedema is a chronic medical condition characterized by a symmetrical buildup of often-painful adipose tissue in the legs, arms and/or lower trunk. (Fig. 1 and Fig. 2)
- Hands/feet are typically spared, sometimes causing the appearance of a "cuff" at the ankle or wrist. (Fig. 1)
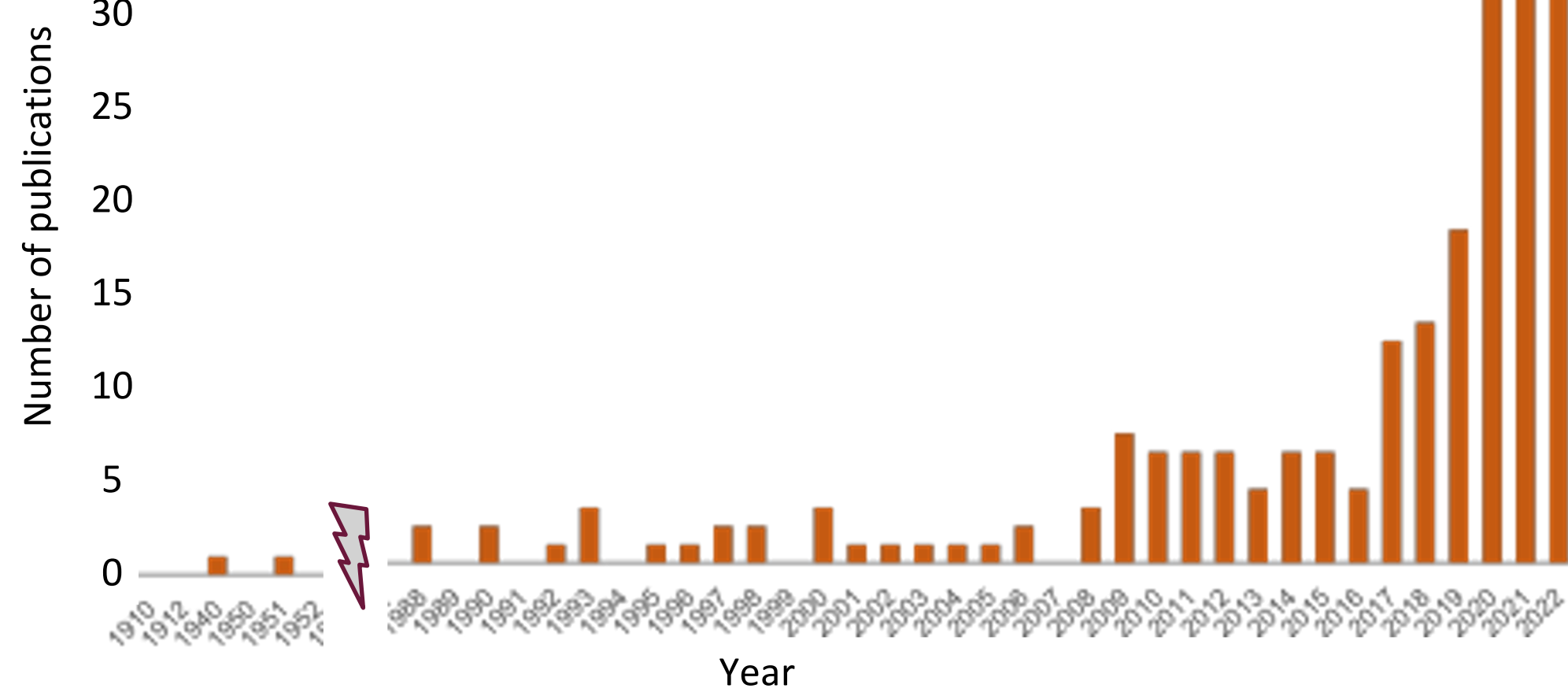

Fig. 1 Lipedema legs at various stages   Fig. 2 Lipedema arms

Table 1:
Growth of Lipedema Primary Data Publications by Year

- Small community of researchers and literature base (Table 1); many are LF funded
- Poor understanding of the biology
- **Objective:** *Create a Roadmap to navigate field wide challenges and provide recommendations on future research*

Lipedema is NOT Obesity

	LIPEDEMA	vs	OBESITY
Areas of excess weight distribution	Extremities sparing hands/feet, can include abdomen*		Entire body
Presence of nodular fat	Yes, especially at later stages		Less common
Tendency to bruise	Frequent		Less likely
Pain associated with fat	Common		Rare
Resistant to dietary interventions and exercise	Common		Less likely
Associated with metabolic or cardiac risks	Less common		More common

Lipedema and obesity may co-occur

*Some patients report Lipedema fat in other locations

Roadmap Methodology

- The roadmap provides recommendations to advance Lipedema research
- Engaged 60+ stakeholders (scientists, clinicians, patients, 11 countries, 24 Reviewers, 1,300 suggestions
- Subset of Key Stakeholders gave extensive feedback on the rough draft of the roadmap
- Key Stakeholders were then asked for additional feedback
- Sections of the Roadmap:
    1. High Quality Research Environment
    2. Standard Lexicon and Best Practices
    3. Diagnostic and Biomarker Tools
    4. Characterizing the Biology of the Disease
    5. Develop Diagnostics
    6. Cultivate Greater Epidemiology Understanding

Results

- Over 140 recommendations for Characterizing the Biology of Lipedema
- Categorized into field specialty, affected systems and body segments

- An example recommendation in adipose biology includes:

    Understand the developmental plasticity of the adipose environment and role of adipose stem cells and progenitors in development—that is, conduct lineage tracing of Lipedema adipocytes
- *In vitro/in vivo* model systems are a great unmet need

Key goals:
- Substantiate field dogma with more rigorous investigation as it is based on multiple hypotheses without significant research backing (Fig. 3)
- Better characterize initiating factors of disease
- Better characterize causes of disease progression

Top Challenges to Overcome:
- Nascent field
- Many specific symptoms are poorly characterized
- Initiation and progression triggers are largely unknown
- Lack of suitable animal and other model systems
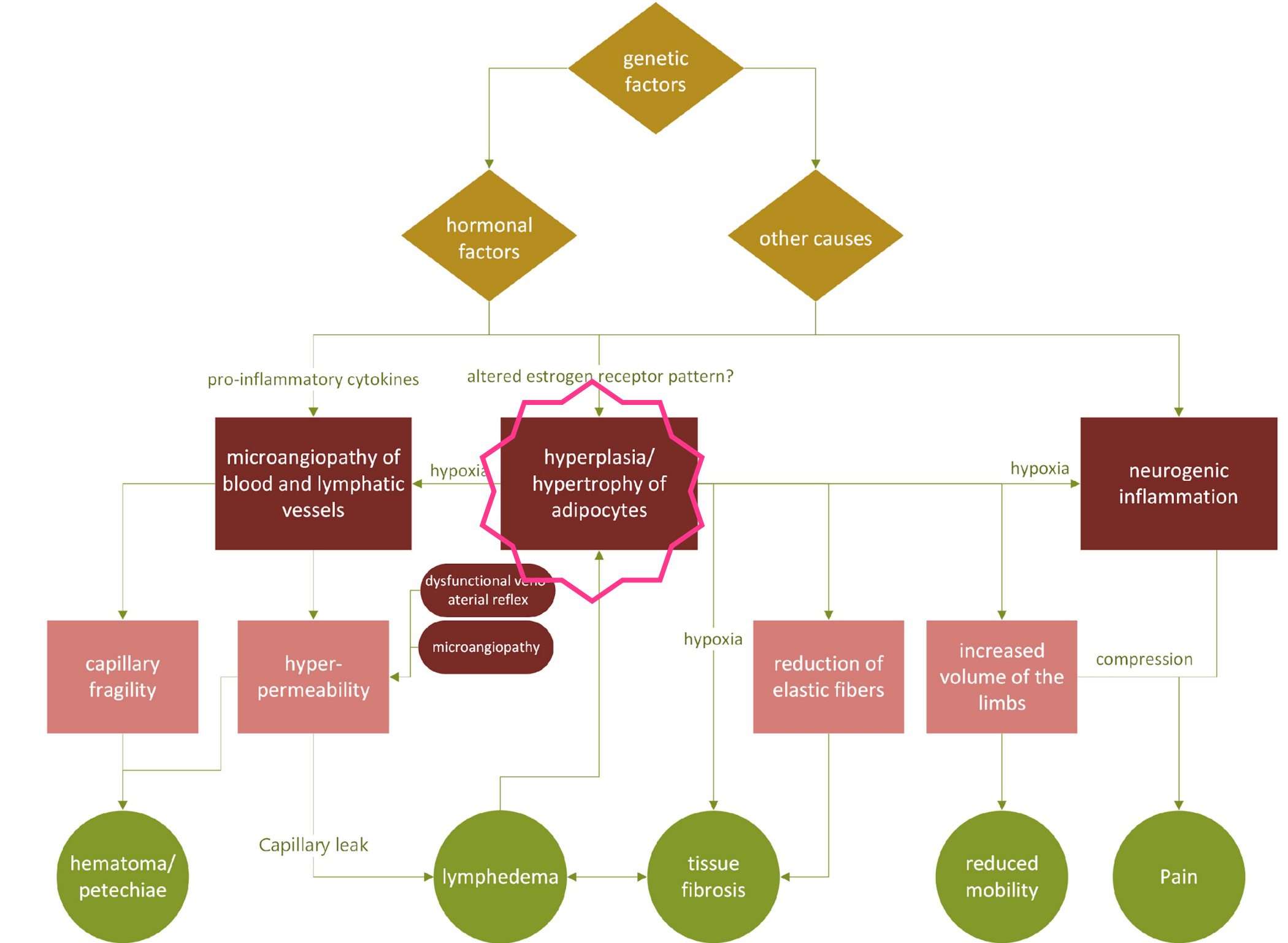
Hypotheses of Lipedema Pathogenesis

Fig. 3. Hypotheses of mechanisms of lipedema pathogenesis
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Conclusion

Top Recommendations in Adipose Biology/Metabolic Changes:
- Understand if dysfunctional adipose is the primary driver of disease
- Conduct lineage tracing of Lipedema adipocytes
- Understand the metabolic changes through progression and consider Lipedema participants as Metabolically Healthy "Obese" (MHO)
- Characterize the adipose depots affecting Lipedema patients
- Investigate the causes/biology of nodular fat

For a copy of the roadmap, visit here: The Lipedema Foundation welcomes comments and suggestions.

LF Funded Research Projects

Lipedema Foundation funds research projects. A list of the current awardees is located here:

If you want to be on our mailing list or for further information, please subscribe to our newsletter at info@lipedema.org

Samples available: Currently, spare tissue from Europe and data from the LF registry. In the future Vanderbilt Biobank will have samples.