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研究課題名(和文) 老化と病態によるリンパ器官の攪乱と免疫応答性の変容

研究課題名(英文) Altered function and structure of immune system in ageing and diseases

研究代表者

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研究成果の概要(和文)：加齢に伴い細胞老化の特徴を示すCD4+ T細胞、SA-T細胞、を発見した。SA-T細胞は、老化関連遺伝子の発現と老化随伴性分泌形質を有し、細胞分裂能の欠質と強い向炎症性因子分泌活性を示した。SA-T細胞はT細胞生成の減少に伴う恒常性増殖による反復性細胞分裂の結果として生成し、自己反応性と強い起炎活性によって、免疫老化形質の主因となる。同細胞は、ループス素因や組織ストレスによっても急増し、全身性自己免疫病や代謝ストレスによる内臓脂肪織炎と糖尿病の発症などを誘導することが示された。本研究により、SA-Tが自己免疫疾患や加齢に伴う慢性組織炎症の発症に重要な役割を果たすことが明らかとなった。

研究成果の概要(英文)：We have identified a CD4+ T-cell population that exhibits cellular senescence features and increases with age (SA-T cells). The SA-T cells expressed senescence-related genes with SA-secretory phenotype (SASP) and showed a potent inflammatory activity with self-reactivity. The SA-T cells are generated after extensive cell divisions in homeostatic proliferation with age. Besides ageing, the SA-T cells are also increased robustly at the lupus-prone background and various tissue stresses and initiate autoimmunity and tissue inflammation such as high fat diet-induced adiposity and insulin-resistance. Current results have revealed that the SA-T cells underlie the systemic autoimmunity and age-related chronic inflammatory disorders.

研究分野：免疫学

キーワード：T細胞 細胞老化 免疫老化 恒常性増殖 老化関連疾患 自己免疫病 慢性炎症

1. 研究開始当初の背景

先進国における高齢化の進行に伴い、加齢に伴う多様な慢性疾患の増加は国民の健康維持の上で大きな社会的問題となっている。加齢関連病態において、獲得免疫応答性低下と炎症性素因や自己免疫リスクの増大によって特徴付けられる免疫老化は重要な基盤的要因となっており、その対応は重要な医学的課題である

2. 研究の目的

本計画研究の目的は、免疫系の老化を免疫系恒常性維持機構と応答性の変容という系統的観点から特に免疫系機能の中枢にあるT細胞系に焦点を当てて解析し、それが個体の恒常性維持と病態発生に与える影響を明らかにすることを目的とする。

3. 研究の方法

免疫系の老化を個体発生の中で全体的に理解するために、免疫系組織および全身のT細胞の動態と恒常性維持の観点から解析し、そのコンテキストの中でT細胞の細胞および分子・遺伝子レベルでの変容に迫る。

4. 研究成果

加齢に伴い細胞老化の特徴を示す CD4⁺ T細胞、SA-T細胞、を発見した。SA-T細胞は、老化関連遺伝子の発現と老化随伴性分泌形質を有し、細胞分裂能の欠質と強い向炎症性因子分泌活性を示した。SA-T細胞はT細胞生成の減少に伴う恒常性増殖による反復性細胞分裂の結果として生成し、自己反応性と強い起炎活性によって、免疫老化形質の主因となる。同細胞は、ループス素因や組織ストレスによっても急増し、全身性自己免疫病や代謝ストレスによる内臓脂肪織炎と糖尿病の発症などを誘導することが示された。本研究により、SA-T が自己免疫疾患や加齢に伴う慢性組織炎症の発症に重要な役割を果たすことが明らかとなった。

5. 主な発表論文等

(研究代表者、研究分担者及び連携研究者には下線)

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[図書] (計 4 件)

〔図書〕(計 件)

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〔産業財産権〕

出願状況 (計 0 件)

取得状況 (計 0 件)

〔その他〕
ホームページ等

6. 研究組織

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