

第6章 総括

この一連の研究で、様々な運動によって起こる白血球の mtDNA の欠失変異を探った。その結果、新たに多くのことが明らかになった。

まず、mtDNA の欠失は健康な若者でも起こることが明らかになった。これまで報告されていた研究成果としては、ミトコンドリア病と呼ばれる特定の疾患患者および高齢者の脳、肝臓、心臓、骨格筋などの組織の mtDNA に、common deletion が蓄積しているというものであった。特に、common deletion は、加齢に伴って指数関数的に増加することが報告されている。今回、このような疾患を持たない健康な若者においても、持久性の運動を行うことによって白血球の mtDNA に common deletion が出現することが示された。

次に、mtDNA の欠失は白血球でも検出できることが明らかになった。すでに述べたように、先行研究のほとんどが、様々な組織から抽出した mtDNA に欠失が蓄積するというものであった。ところが、本研究では白血球から抽出した mtDNA を用いて common deletion を検出することができた。これは、健康なヒトを被験者にした実験を行う場合、被験者の身体的苦痛を軽減することにつながるため、大きなメリットとなる。

次に、この common deletion の出現は、様々な運動によって同様に起こることが明らかになった。この一連の研究で行った運動としては、ジョギング、自転車エルゴメータによる運動、シャトルランテスト、バスケットボールの練習および合宿練習など、様々な持久的運動であったが、それらの運動を行うことによって白血球の mtDNA に common deletion が出現したことが示された。さらに、筋力トレーニングによってもこの欠失が出現しており、持久性の運動だけでなく、運動全般において同様の状況が起こる可能性が示唆された。

次に、比較的軽い運動負荷であっても mtDNA に common deletion が出現することが明らかになった。先行研究では、ラットに急激な運動をさせることによって、骨格筋中のミトコンドリアに変性が起こり、また骨格筋の mtDNA には欠失が出現することが報告されていたが、本研究の場合では、50% VO₂max 程度の比較的軽い運動負荷であっても白血球の mtDNA に common deletion が出現したことが示された。

次の発見は、白血球の mtDNA に common deletion が出現するかどうかに関して、欠失変異を引き起こす運動負荷には閾値がありそうであることがうかがえた。しかし、この点に関しては、本研究では完全には明らかになっていない。まず、短期間のベッドレストにより身体活動量を制限した場合には欠失が出現しないことがわかった。さらに、40 W の負荷で自転車エルゴメータによる運動を 30 分間行った場合には欠失が出現しないが、80 W の負荷の運動では欠失が出現したという結果から、この 40 W と 80 W の負荷の間に欠失変異を出現させるような閾値が存在する可能性が示唆される。

なお、補足的な発見ではあるが、欠失は運動終了から数日後に起こることが明らかになった。従来の 8-OH-dG をバイオマーカーとした実験結果では、運動直後からこの量が増大し、数時間後には運動前の値に戻ることが報告されているが、mtDNA の欠失は運動直後ではなく、運動終了から 2～3 日後に出現することが明らかになった。

さらに、本研究では出現した common deletion の動態についても観察したが、common deletion は蓄積することなく、4～5 日後に消失することが明らかになった。これについては、検体として白血球を用いた研究であったことによるためであるか、健康な若者を被験

者に用いているためであるかなど、本研究では明らかにならない点があるが、いずれにしても欠失が消失することは重要なポイントである。特に、運動によってDNA修復酵素の活性が高まることが報告されており、今回の研究からも運動前に見られていた mtDNA の common deletion が運動から数日後に消失したことから、適度な運動を行うことによって変異した mtDNA の修復能力が高まることが期待できる。これはまた、運動を行うことによって健康の維持・増進を図ることの重要な根拠となりうる。

なお、今後の研究の方向性として、変異した mtDNA を定量することが課題であるといえる。この一連の研究では、ネスト PCR 法により変異 mtDNA を増幅したことによって、わずかな量の common deletion の有無を検出することができた。そのため、この方法では、変異した mtDNA の量を定量することが困難である。したがって、この定量化が可能となれば、この分野の研究が飛躍的に進展するものと思われる。この点に関しては、今後の技術革新に期待することになろう。

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