剤の形状・様態、投与対象の状態、疾患の種類、適用部位、細胞微少環境なども臨床上での腫瘍発生可能性の関連要因であるが、これらをすべて包含した上での外挿性を語るのは現時点できわめて困難である。

(13) 造腫瘍試験はどこまで必要か？体性幹細胞由来製品では動物を用いた試験は不要では？製品の（通常の培養期間、倍加時間、継代数を超える培養時）の増殖曲線などから担保することで良いのではないか（培地、培養条件が課題）。多能性幹細胞の場合は製品レベルでは未分化細胞の残存がまず問題だが、これには、とりあえず、未分化細胞特有の遺伝子発現を高感度なPCR で検出する方策や（製品の）通常を超える培養時による細胞増殖評価。次いで動物試験。（iPS 細胞等由来特定製品で、ある種の遺伝子発現と分化異常、あるいはカルシテラトーマ発現頻度の高さなどの因果関係が明らかな場合は、当該遺伝子発現を検討するのは意味あるかも知れない）。本格的には次年度の課題。

(14) 関心事項はなるべくある種の結論を得るべく努力し、公表するが、ガイドライン化した方が良い事項（一般的で共通的な事項）とQA、補遺などで解説した方が良い事項がある。後者には個別製品の上乗せ部分に関わる事項が多い（例示する）。

(15) 非臨床試験における動物モデル製品とモデル動物の効用。本来のヒト製品と異なる製品を製造しなければならない手間と出来た製品の妥当性をいかに担保するかなどの問題がつきまとう。動物モデル製品は有効性試験については一定の妥当性が考えられるが、安全性試験については、どうか？

(16) いわゆる毒性試験よりも一般薬理試験的なものの方が妥当性は高いのでは。

(17) ある課題の解決策にはケースに応じた多様な答えがある。注釈、説明等をつけながら、何らかの形で公表し、認識できるようにする。

### C-7 MCP コンセプトの国際発信

本研究は、あらゆる製品に最低限必須・共通の要件や基準・評価技術（ミニマム・コンセンサス・パッケージ：ＭＣＰ）を提言し、より合理的、効率的、効果的な製品開発を促進し、再生医療実用化の推進に寄与することを目的としている。ＭＣＰは、これを共通のプラットホームとし、これに各製品の特性等を踏まえた技術的要件を選択して上乗せする、という合理的アプローチを可能にする特色を持つ独創的なものであり、諸外国では類をみず、規制面から国際的

優位性を確保するための方策である。その一方で、こうした方策が世界レベルで認知されること、ひいては世界の標準的アプローチになれば、これに勝るものはない。おりしも、2015年2月18-19日に東京において、International Alliance for Biological Standardization, PMDA, JST, NIBIO, WHOにより“International Regulatory Endeavor towards Sound Development of Human Cell Therapy Products”と題された国際シンポジウムが開催された。本国際会議の運営委員会には、本研究班代表の早川（委員長）の他、研究分担者である青井、梅澤、佐藤、松山、大和が主要メンバーとして参画しており、MCPをメインテーマの一つとして設定した。ここでMCPプラスケース別上乗せ方策のコンセプト及び事例一般（早川堯夫）、規格及び試験方法（早川堯夫・坂本典久）、iPS細胞（青井貴之）、ES細胞・非臨床有効性（梅澤明弘）、非臨床安全性（松山晃文）、造腫瘍性（佐藤陽治）、臨床評価と課題（大和雅之・矢野一男）、GXP（佐藤大作）、生物由来原材料（前田大輔）その他についてそれぞれわが国関係者が講演し、国際発信した。このうち、MCPプラスケース別上乗せ方策のコンセプト及び事例一般（早川堯夫）のスライド１－64を収載する（スライド1-64）。

## D．考察

本年度の研究では、１）あらゆる製品の試験や評価の際に適用すべき共通の一般的留意事項（一般原則）、２）（改正薬事法）及び再生医療安全性確保法下における、細胞・組織を取り扱う上での最低限必須・共通の技術的・倫理的留意事項や技術要件（GTP（Good Cell/Tissue Practice）のＭＣＰ），３）製品の製造方法と品質（試験・評価・管理）に関するMCP、４）非臨床安全性試験におけるＭＣＰ、５）非臨床有効性（ＰＯＣ）試験におけるＭＣＰなどを案出した。これらMCPは必要に応じてガイドライン化されるべきものである。しかし、一般原則、GTP, 製品の製造方法と品質については具体的なMCP提案が可能と思われるが、非臨床安全性・有効性試験部分では、むしろケース別にどのような対応すべきかを英知を結集して考案しなければならないところが多いと考えられる。

いずれにしても。MCPを共通のプラットホームとし、次に製品の種類・特性、対象疾患、開発段階を考慮し、既存の網羅的指針等を参考にしつつ、当該ケースに応じて上乗せすべき試験・評価項目を選択するというアプローチを適用すれば、学・産の研究・開発の実施、官での薬事戦略相談などの円滑な進行、再生医療安全確保法下でのヒト幹臨床研究等の薬機法下での開発への切れ目のない移行、的確な承認審査などが可能となる。その結果、再生医療等製品の品質及び安全性を確保しつつ、合理的、効率的、効果的な製品開発を促進し、再生医療の実用化の推進に寄与することによ

り、厚生労働行政上きわめて大きな意義を持つと期待される。わが国が欧米を上回るスピードで実用化していくためにも研究成果の果たす役割は大きい。

## E. 結論

MCP は再生医療等安全性確保法下でのヒト特定細胞加工物の利用から薬機法の下でのヒト細胞加工製品の開発への切れ目のない移行、行政での薬事戦略相談や承認審査などの円滑な進行を可能にする共通のプラットホームともなる。欧米ではこのようなアプローチは系統化されていない。わが国が今後、わが国のシーズを欧米を上回るスピードで実用化していくためには、系統化されたガイダンスの存在や今回提言するアプローチの活用がきわめて大きな役割を果たすと考えられる。将来的にはこのアプローチが WHO 等に採択され、世界標準の一つとなる可能性も期待される。

## F. 健康危険情報

特記事項なし

## G. 研究発表

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